Docket No.: F2842 US S3 (C018016/0180304)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)

Michael BARDROFF *et al.*)

Serial No.: 10/505,313)

Filed: August 20, 2004)

Examiner: G. S. Emch

Art Unit: 1649

For: **ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE**

New York, New York
October 14, 2009

REQUEST FOR RECONSIDERATION OF PATENT TERM ADJUSTMENT UNDER 37 CFR § 1.705(b)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Request For Reconsideration Of Patent Term Adjustment Under 37 CFR § 1.705(b) ("Request") is being filed in response to the Notice of Allowance and Fee(s) Due ("Notice") and Notice of Allowability mailed August 21, 2009. The Determination of Patent Term Adjustment Under 35 U.S.C. § 154(b) mailed with those papers indicates that the adjustment is only for ***95 days***. We respectfully request reconsideration of this Determination.

The instant patent application was filed under 35 U.S.C. 371 on August 20, 2004. The Patent Term Adjustment History, as displayed on the PAIR system, is attached hereto as Exhibit A. Applicants do not address herein the Office's calculation

of patent term adjustment under 35 U.S.C. § 154(b)(1)(A).[1] Applicants, however, respectfully request reconsideration of the Office's calculations of the patent term adjustment under 35 U.S.C. § 154(b)(2)(C). Specifically, Applicants respectfully request that the ***198*** day delay related to the submission of a response to a non-final Office Action (received in the Office on January 16, 2009) (the "January 16, 2009 Response") be reconsidered and reduced to ***2*** days. Thus, Applicants respectfully submit that the patent term adjustment is at least ***291*** days – a difference of ***196*** days from the Office's assessment of ***95*** days.

This Request is being filed before payment of the issue fee and is therefore timely. 37 CFR § 1.705(b).

We enclose a check for $200.00 to cover the applicable fee. 37 CFR §§ 1.705(b)(1) and 1.18(e). Please charge any required fees not otherwise paid by check to Deposit Account No. 02-4467. A copy of this sheet is enclosed.

Facts of the Case

The facts of the case are listed below, with the portions most relevant to this Request for Reconsideration underlined.

- The application entered U.S. national stage on August 20, 2004.

[1] We note that because the application has not issued, patent term adjustment under 35 U.S.C. § 154(b)(1)(B) cannot be calculated as of this time. Indeed, the Patent Term History displayed on the PAIR system does not show a calculation under 35 U.S.C. § 154(b)(1)(B). Furthermore, on September 14, 2009, Mr. Mark Polutta of the Office of Legal Administration at the USPTO confirmed that patent term adjustment under 35 U.S.C. § 154(b)(1)(B) will be calculated only after the patent issues. Accordingly, Applicants do not raise issues related to or under 35 U.S.C. § 154(b)(1)(B) at this time but reserve the right to do so after issuance.

of patent term adjustment under 35 U.S.C. § 154(b)(1)(A).[1] Applicants, however, respectfully request reconsideration of the Office's calculations of the patent term adjustment under 35 U.S.C. § 154(b)(2)(C). Specifically, Applicants respectfully request that the ***198*** day delay related to the submission of a response to a non-final Office Action (received in the Office on January 16, 2009) (the "January 16, 2009 Response") be reconsidered and reduced to ***2*** days. Thus, Applicants respectfully submit that the patent term adjustment is at least ***291*** days – a difference of ***196*** days from the Office's assessment of ***95*** days.

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- The application entered U.S. national stage on August 20, 2004.

[1] We note that because the application has not issued, patent term adjustment under 35 U.S.C. § 154(b)(1)(B) cannot be calculated as of this time. Indeed, the Patent Term History displayed on the PAIR system does not show a calculation under 35 U.S.C. § 154(b)(1)(B). Furthermore, on September 14, 2009, Mr. Mark Polutta of the Office of Legal Administration at the USPTO confirmed that patent term adjustment under 35 U.S.C. § 154(b)(1)(B) will be calculated only after the patent issues. Accordingly, Applicants do not raise issues related to or under 35 U.S.C. § 154(b)(1)(B) at this time but reserve the right to do so after issuance.

- The application fulfilled the requirements of 35 U.S.C. § 371 on March 7, 2005.
- A Requirement for Restriction/Election was mailed on June 5, 2007.
- A response to the Requirement for Restriction/Election was received by the Office on July 27, 2007.
- A First Supplemental IDS was received by the Office on August 6, 2007.
- An Office Communication was mailed on October 18, 2007.
- A Response to the October 18, 2007 Office Communication was received by the Office on October 25, 2007.
- A Second Supplemental IDS was received by the Office on November 13, 2007.
- A non-final Rejection was mailed on January 28, 2008 (the "January 28, 2008 Office Action"). Exhibit B attached hereto is a copy of the January 28, 2008 Office Action.
- A Response to January 28, 2008 Office Action with a properly executed certificate of mailing and a two-month extension of time was timely mailed on June 30, 2008. The PTO received the Response on July 2, 2008 (the "July 2, 2008 Response"). Exhibit C attached hereto is a copy of the main text of the July 2, 2008 Response (without the Exhibit attached thereto) along with a date-stamped postcard evidencing such receipt.

- An Examiner Interview was conducted on July 9, 2008. An Interview Summary recording the substance of that Interview was mailed on July 28, 2008 (the "July 28, 2008 Interview Summary"). Exhibit D attached hereto is a copy of the July 28, 2008 Interview Summary.
- A Supplemental Response to the Office Action with a properly executed certificate of mailing and a three-month extension of time was timely mailed on July 24, 2008 in response to the January 28, 2008 Office Action. The PTO received the Response on July 28, 2008 (the "July 28, 2008 Supplemental Response"). Exhibit E attached hereto is a copy of the July 28, 2008 Supplemental Response along with a date-stamped postcard evidencing such receipt.
- An Office Communication was mailed on October 14, 2008 (the "October 14, 2008 Office Action"). Exhibit F attached hereto is a copy of the October 14, 2008 Office Action.
- A Response to the October 14, 2008 Office Action with a properly executed certificate of mailing and a two-month extension of time was timely mailed on January 13, 2009. The PTO received the Response on January 16, 2009 (the "January 16, 2009 Response"). Exhibit G attached hereto is a copy of the January 16, 2009 Response along with a date-stamped postcard evidencing such receipt.
- A Third Supplemental IDS was received by the Office on January 21, 2008.

- A Final Office Action was mailed on April 29, 2009. Exhibit H attached hereto is a copy of the Final Office Action.
- A response to the April 29, 2009 Final Office Action was received by the Office on July 31, 2009.

Review of Patent Term Adjustment Calculation

The Office treated the July 2, 2008 Response as a submission of a reply having an omission (*See* Patent Term Adjustment History, "07-02-2008 Informal or Non-Responsive amendment after Examiner Action"). Furthermore, the January 16, 2009 Response was treated as a paper correcting a reply having an omission. Thus, according to the Office, the period of delay was from July 3, 2008 to January 16, 2009, or 198 days (37 CFR § 1.704(c)(7)). Indeed, the Patent Term Adjustment History shows a 198 day delay associated with the January 16, 2009 Response.

At issue is whether the claims submitted in the July 2, 2008 Response, and amended and prosecuted thereafter, embraced the elected "MSR-7" species. Dispositive of the issue is the Final Action, in which the Examiner explicitly acknowledged that the claims presented previously and then amended always read on the necessary MSR-7 sequences: "The examiner agrees that claim 1 and dependent claims still encompass the elected antibody of MSR-7." (Paper No. 20090422 at 3, emphasis added).

As the record reflects and as detailed below, the evident confusion arose because the sequence listing included multiple different SEQ ID Nos. for individual identical sequences, and the Examiners and Applicants unfortunately focused upon

different SEQ ID Nos. when it came to the issue of the elected MSR-7 species. When the record is studied, it will be appreciated (as the Examiners did during examination) that Applicants properly responded to the restriction requirement and that subsequent clarifying claim amendments were simply that, *i.e.,* for clarification, not for correcting an omission.

The alleged omission is that the claims failed to include the elected MSR-7 species.

The October 14, 2008 Office Action indicated that a reply has an omission which must be corrected, and thus appeared to be an Office Action issued under 37 CFR 1.135(c)(3). In this Office Action, the Examiner alleged that the **July 28, 2008 Supplemental Response** "canceling all claimed subject matter drawn to the elected invention and presenting only claims drawn to a non-elected invention is non-responsive." (Paper No. 20081009 at 1).

The Examiner asserted that "[a]ccording to Applicants' specification (e.g. Figure 4 and sequence listing), the 6 CDR sequences for the elected MSR-7 antibody are L-CDR1=SEQ ID NO: 143, L-CDR2=SEQ ID NO: 144, L-CDR3=SEQ ID NO: 18, H-CDR1=SEQ ID NO: 146, H-CDR2=SEQ ID NO: 147 and H-CDR3=SEQ ID NO: 24." (*Id.*) The Examiner concluded, "[t]hus, newly amended claim 1 and newly presented claim 41 (as of [the] amendment dated **02 July 2008**) and dependent claims are directed to an invention(s) that is independent or distinct from the invention originally claimed because none of the claims encompass the CDR sequences of the elected MSR-7 species." (*Id.*, emphasis added) The Examiner further asserted "[s]ince the above-mentioned amendment appears to be a bona fide attempt to reply, applicant is

given a TIME PERIOD of ONE (1) MONTH or THIRTY (30) DAYS, whichever is longer, from the mailing date of this notice within which to supply the omission or correction in order to avoid abandonment." (*Id.*)

Thus, in the October 14, 2008 Office Action, the Examiner alleged that the July 28, 2008 Supplemental Response is non-responsive in view of the restriction requirement and gave details as to the nature of the omission—that the 6 CDR sequences of the elected MSR-7 species were not included in the amended claims. We note, however, it was not clear whether the Examiner also alleged that the earlier July 2, 2008 Response was non-responsive for the same reason as well, because the July 2, 2008 Response was mentioned in the context of the allegation that "none of the claims encompass the CDR sequences of the elected MSR-7 species" (Paper No. 20081009 at 1).

As we will show below, neither response had an omission as alleged by the Examiner.

The July 2, 2008 Response did not have an omission.

It is respectfully submitted that the amended claims of the July 2, 2008 Response encompassed the elected species of MSR-7, and thus, it is not a reply having an omission.

Examination of the July 2, 2008 Response reveals that it was fully responsive, not nonresponsive, because the particular SEQ ID NOs for MSR-7 mentioned by the Examiner on page 1 of Paper No. 20081009 were recited in amended independent claim 1 of the July 2, 2008 Response, as highlighted in bold below:

Claim 1. An antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/Aβ4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof, wherein said antibody molecule comprises

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 96, 130-133, 141-**143**, 160, 175-177, 180, 189, 190, 200, 201, 206-211, and 224;

(2) L-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 97, **144**, 161, and 212; and

(3) L-CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 16, **18**, 20, 75, 77, 79, 81, 83, 85, 87, 95, 98, 102, 103-107, 145, 149-159; 162, 166, 178, 183, 202, 213, 217, 218, 220, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411 and 413; and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 99, **146**, 163, 203, and 214;

(2) H-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 100, 108-129, 134-140, **147**, 164, 167-174, 179, 181, 182, 184-188, 191-199, 204, 205, 215, 219, and 221-223; and

(3) H-CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 22, **24**, 26, 61, 63, 65, 67, 69, 71, 73, 93, 101, 148, 165, 216, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, and 383. (The July 2, 2008 Response at 10, emphasis added.)

Because many SEQ ID Nos. were recited in amended claim 1, Applicants were invited at the Examiner Interview of July 9, 2008 to **clarify** or to **explain** "how the newly submitted claim amendments read on the elected invention." (Paper No. 20080718 at 1). This invitation to clarify was memorialized in the July 28, 2008 Interview Summary, which states:

> The examiners informed applicants' representative that it is unclear how the newly submitted claim amendments read on the elected invention. It was proposed that Applicants' representatives submit a subsequent response to address this issue. (Paper No. 20080718 at 1, emphasis added).

Thus, it is clear that the July 2, 2008 Response did not omit an elected species in response to the restriction requirement, and it is respectfully submitted that the July 2, 2008 Response should not be characterized as having an omission that falls under 37 CFR § 1.704(c)(7).

The July 28, 2008 Supplemental Response is a supplemental response expressly requested by the Examiners and does not contain an omission.

While the Examiner alleged in the October 14, 2008 Office Action that there is an omission in the July 28, 2008 Supplemental Response, it is respectfully submitted that the July 28, 2008 Supplemental Response did not contain such an omission. The omission alleged by the Examiner, as detailed above and as set forth by the Examiner in the October 14, 2008 Office Action, is that none of the claims contain the 6 CDR sequences for the elected species. (Paper No. 20081009 at 1).

As we explained in an Examiner Interview on December 3, 2008, however, and as memorialized in the January 16, 2009 response, amended claim 1 of the July 28, 2008 Supplemental Response recites the six CDR sequences of MSR-7 antibody. The confusion was due to the fact that the six SEQ ID NOs. recited in claim 1 for the six CDRs of MSR-7 were different from the SEQ ID NOs. noted by the Examiner, because the sequence listing included redundant SEQ ID NOs. for the same CDR sequences. In an effort to simplify the claim in response to the Examiners' invitation

during the July 9 interview, we deleted the redundant SEQ ID NOs., including, unfortunately, the particular SEQ ID NOs. recited by the Examiner in the October 14, 2008 Office Action. Still recited in the claim, however, as they had always been, were the sequences of the six CDRs of the elected MSR-7 species.

Indeed, in the Final Office Action attached hereto as Exhibit 7, the Examiner acknowledged that "Applicants' arguments have been fully considered and are found persuasive. The examiner agrees that claim 1 and dependent claims still encompass the elected antibody of MSR-7." (Paper No. 20090422 at 3, emphasis added). Therefore, it is respectfully submitted that the amended claims in the July 28, 2008 Response was responsive and that this Response did not contain an omission under 37 CFR § 1.704(c)(7), either.

Instead of characterizing the July 28, 2008 Supplemental Response as a reply having an omission, it is respectfully submitted that the July 28, 2008 Supplemental Response was a supplemental reply (1) expressly requested by the Examiner and (2) correcting an oversight or misunderstanding by the Examiner, an oversight ultimately acknowledged by the Examiner. See also the first paragraph on page 2 of the July 28, 2008 Supplemental Response: "During the interview, the Examiners noted the restriction requirement and the search requirements implicated by the previously amended claims and requested additional amendments and/or remarks to facilitate examination of the elected subject matter." Because the July 28, 2008 Supplemental Response was a supplemental response expressly requested by the Examiners, it falls within the exception set forth in 37 CFR § 1.702(c)(8) and therefore,

this is an additional reason that the period of time between its submission and that of the July 2, 2008 Response is not subject to reduction of the patent term adjustment.

Applicants' Patent Term Adjustment Calculation

Based on the foregoing, applicants are entitled to a patent term adjustment of **291** days under 37 CFR §§ 1.703(a), 1.704(b), and 1.704(c)(8), because (1) neither the July 2, 2008 Response nor the July 28, 2008 Response contained an omission under 37 CFR § 1.704(c)(7), and (2) the PTO erred in calculating the patent term adjustment.

The requested adjustment of **291** days is calculated according to the formulas set forth in 37 CFR § 1.703 (a)(1) and §§ 1.704(b) and (c)(8):

Ground for Adjustment	Number of days	Explanation
§ 703(a)	394	May 8, 2006 (the day after the date that is fourteen months after the date the application fulfilled the requirements of 35 U.S.C. § 371) to June 5, 2007 (the date of mailing of the Restriction Requirement).
§ 704(c)(8)	10	July 28, 2007 (the day after the date that a response was received in the Office) to August 6, 2007 (the submission of the First Supplemental IDS)
§ 704(c)(8)	19	October 26, 2007 (the day after the date that a response was received in the Office) to November 13, 2007 (the submission of the Second Supplemental IDS)
§ 704(b)	65	April 29, 2008 (the day after the date that is three

Ground for Adjustment	Number of days	Explanation
		months after the January 28, 2008 Office Action was mailed) to July 2, 2008 (the date the Response was received in the Office)
§ 704(b)	2	January 15, 209 (the day after the date that is three months after the October 14, 2008 Office Action was mailed) to January 16, 2009 (the date the Response was received in the Office)
§ 704(c)(8)	5	January 17, 2009 (the day after the date that a response was received in the Office) to January 21, 2009 (the submission of the Third Supplemental IDS)
§ 704(b)	2	July 30, 2009 (the day after the date that is three months after the April 29, 2009 Final Rejection was mailed) to July 31, 2009 (the date the Response to the Final Office Action was received in the Office)

As shown by our calculations, the term for the allowed patent should be **291** days (394-10-19-65-2-5-2=291), not just 95 days.

Terminal Disclaimer

Upon information and belief, the undersigned represents that the patent to issue based on the above-identified application is not subject to a terminal disclaimer (37 CFR § 1.705 (b)(2)(iii)).

Summary

For the foregoing reasons, applicants respectfully request that **291** days be added to the term of the patent (instead of 95 days).

Please contact the undersigned if there are any questions regarding this paper.

I hereby certify that this correspondence (including the check and other papers identified as being enclosed) is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-14501, on October 14, 2009.

Jihong Zang, Reg. No. 56,606

Respectfully submitted,

By: _____

Stephen M. Haracz
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10/505,313 ANTI-AMYLOID BETA ANTIBODIES

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Patent Term Adjustment

Filing or 371(c) Date:	03-07-2005	USPTO Delay (PTO) Delay (days):	394
Issue Date of Patent:	-	Three Years:	-
Pre-Issue Petitions (days):	+0	Applicant Delay (APPL) Delay (days):	299
Post-Issue Petitions (days):	+0	Total Patent Term Adjustment (days):	95
USPTO Adjustment (days):	+0	Explanation Of Calculations	

Patent Term Adjustment History

Date	Contents Description	PTO(Days)	APPL(Days)
08-21-2009	Mail Notice of Allowance		
08-19-2009	Document Verification		
08-19-2009	Notice of Allowance Data Verification Completed		
08-19-2009	Case Docketed to Examiner in GAU		
08-14-2009	Examiner's Amendment Communication		
06-17-2009	Examiner Interview Summary Record (PTOL - 413)		
07-31-2009	Information Disclosure Statement considered		
07-31-2009	Information Disclosure Statement (IDS) Filed		
08-05-2009	Date Forwarded to Examiner		
07-31-2009	Amendment after Final Rejection		2
07-31-2009	Information Disclosure Statement (IDS) Filed		↑
04-29-2009	Mail Final Rejection (PTOL - 326)		↑
12-03-2008	Examiner Interview Summary Record (PTOL - 413)		
04-27-2009	Final Rejection		
01-21-2009	Information Disclosure Statement considered		
01-21-2009	Information Disclosure Statement (IDS) Filed		5
02-04-2009	Date Forwarded to Examiner		↑
01-16-2009	Response after Non-Final Action		198
01-16-2009	Request for Extension of Time - Granted		↑
01-21-2009	Information Disclosure Statement (IDS) Filed		↑
10-14-2008	Mail Notice of Informal or Non-Responsive Amendment		↑
08-12-2008	CRF Is Good Technically / Entered into Database		↑
08-08-2008	Date Forwarded to Examiner		↑
07-28-2008	Supplemental Response		↑
08-08-2008	Date Forwarded to Examiner		↑
07-02-2008	Informal or Non-Responsive Amendment after Examiner Action		↑
07-02-2008	Response after Non-Final Action		65
07-02-2008	Request for Extension of Time - Granted		↑
07-28-2008	Mail Examiner Interview Summary (PTOL - 413)		↑
07-28-2008	Mail Miscellaneous Communication to Applicant		↑
07-09-2008	Examiner Interview Summary Record (PTOL - 413)		↑
06-13-2008	Miscellaneous Communication to Applicant - No Action Count		↑
01-28-2008	Mail Non-Final Rejection		↑
01-22-2008	Non-Final Rejection		
11-13-2007	Information Disclosure Statement considered		
11-13-2007	Reference capture on IDS		
11-13-2007	Information Disclosure Statement (IDS) Filed		19
11-13-2007	Information Disclosure Statement (IDS) Filed		↑
11-07-2007	Date Forwarded to Examiner		↑
10-25-2007	Response after Non-Final Action		↑
10-18-2007	Mail Miscellaneous Communication to Applicant		

10-15-2007	Miscellaneous Action with SSP		
08-06-2007	Information Disclosure Statement considered		
10-10-2007	Case Docketed to Examiner in GAU		
08-06-2007	Reference capture on IDS		
08-06-2007	Information Disclosure Statement (IDS) Filed		10
08-06-2007	Information Disclosure Statement (IDS) Filed		↑
08-04-2007	Date Forwarded to Examiner		↑
07-27-2007	Response to Election / Restriction Filed		↑
07-27-2007	Request for Extension of Time - Granted		
06-05-2007	Mail Restriction Requirement	394	
05-29-2007	Requirement for Restriction / Election	↑	
12-14-2005	Case Docketed to Examiner in GAU	↑	
09-20-2005	IFW TSS Processing by Tech Center Complete	↑	
09-20-2005	Case Docketed to Examiner in GAU	↑	
03-07-2005	Oath or Declaration Filed (Including Supplemental)	↑	
04-11-2005	Cleared by OIPE CSR	↑	
03-07-2005	371 Completion Date	↑	
03-30-2005	Application Dispatched from OIPE		
03-30-2005	Notice of DO/EO Acceptance Mailed		
03-07-2005	Additional Application Filing Fees		
03-07-2005	A statement by one or more inventors satisfying the requirement under 35 USC 115, Oath of the Applic		

If you need help:

- *Call the Patent Electronic Business Center at (866) 217-9197 (toll free) or e-mail EBC@uspto.gov for specific questions about Patent Application Information Retrieval (PAIR).*
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,313	03/07/2005	Michael Bardroff	F2842 US S3 (C018016/0180	1924

7590 01/28/2008

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1290 Avenue of the Americas
New York, NY 10104-3300

EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
01/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,313	BARDROFF ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007 and 25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-16,22 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-16,22 and 28-30* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-9,11-16,22 and 28-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/20/04, 8/6/07, 11/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' elections with traverse of Group I, claims 1-16, 22 and 28-30, and of species B) MSR-7 antibody, in the reply filed on 27 July 2007 are acknowledged. Because applicants did not distinctly and specifically point out the supposed errors in the restriction and election of species requirements, the elections have been treated as elections without traverse (MPEP § 818.03(a)).

Response to Amendment

Claims 10, 17-21, 23-27 and 31-40 have been canceled as requested in the amendment filed on 25 October 2007. Following the amendment, claims 1-9, 11-16, 22, and 28-30 are pending in the instant application.

Claims 1-9, 11-16, 22, and 28-30 are under examination in the instant office action.

Sequence Rules Requirement

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Therefore, the application must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Therefore, the application must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). However the

instant application is not in compliance with the sequence rules, particularly 37 C.F.R. § 1.821(d), which requires that reference be made to a particular sequence identifier (SEQ ID NO:) in the specification and claims at each disclosure of a sequence encompassed by the definitions set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). The instant claim 3 and supporting sections of the specification contain sequences, which are not properly identified.

In case these sequences are new, Applicants must provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification wherever a reference is made to that sequence. For rules interpretation Applicants may call (703) 308-1123. See M.P.E.P. 2420-2435. Applicants are advised to review the entire text of the instant specification for compliance with sequence rules.

Information Disclosure Statements

Signed and initialed copies of the IDS papers filed on 20 August 2004, 06 August 2007 and 13 November 2007 are enclosed in this action.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies or fragments thereof that comprise 6 CDRs, three from the VH domain and three from the VL domain, wherein the antibodies and fragments thereof bind the same antigen as claimed, does not reasonably provide enablement for an antibody and fragments thereof that do not contain a full set of 6 CDRs from the VH and the VL domains as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative

skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

Claims 4-6 are broadly drawn to antibodies or fragments thereof, comprising only a VH and/or a VL domain that do not contain a full set of 6 CDRs from the VH and the VL domains.

The specification discloses only antibodies that contain both a VH and a VL chain with no less than 6 CDRs, 3 from the VH chain and 3 from the VL chain that bind to antigen (see Table 1, pp.64-68). The specification does not enable antibodies and fragments thereof, which do not contain 6 CDRs and bind antigen.

It is well established in the art that the formation of an intact antigen-binding site of all antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope (Paul, Fundamental Immunology, (textbook), 1993, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions"). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites (Paul, page 293, first

column, lines 3-8 and line 31 to column 2, line 9 and lines 27-30). Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA 1982 Vol. 79: page 1979). The Rudikoff et al. reference teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that the antibodies and fragments thereof as defined by the claims, which may contain less than the full complement of CDRs from the heavy and light chain variable regions have the required binding function. Applicants have provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability of producing an antibody and fragments thereof containing fewer than 6 CDRs, resulting in an antibody that retains the antigen specificity currently claimed. However, the claim language also reads on small amino acid sequences, which are incomplete regions of the variable region of the antibody. One of skill in the art would neither expect nor predict the appropriate functioning of the antibodies as broadly as is claimed. Therefore, in view of the lack of guidance in the specification and in view of the discussion above, undue experimentation would indeed be required to make and use the invention commensurate with the scope of the claims.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it

The invention appears to employ novel biological materials, specifically the MSR-3; MSR-7 and MSR-8 antibodies. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. It appears that Applicants have not deposited the biological materials, and a deposit at a recognized depository may be made for enablement purposes. If a deposit has been made under the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, and that the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicants' attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information; however, Applicants are cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicants are advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection
10801 University Boulevard
Manassas, VA 20110-2209

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims depend from canceled claims, i.e. claims 17 and 18 and 27, respectfully. Thus, the metes and bounds of claims 22 and 28 cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 8, 9, 15, 16, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,955,317 to Suzuki et al (citation A3 on the IDS dated 13 November 2007.

The claims are directed to an antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/A β4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof

and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof.

The Suzuki et al. patent teaches a monoclonal antibody that specifically recognizes two regions of the β-amyloid (i.e., β-A4) peptide, wherein the two regions are the amino acid sequences of SEQ ID NO: 7 and SEQ ID NO: 10 (see claim 1, for example). The Suzuki et al. patent's SEQ ID NO: 7 is the amino acid sequence DAEFRHDSGYEVHHQKLVFFAEDVGSNK, which comprises both the instant SEQ ID NO: 1 and the instant SEQ ID NO: 2 (see cols. 47-48), and the Suzuki et al. patent's SEQ ID NO: 10 is the amino acid sequence DAEFRHDSGYEVHHQK, which comprises the instant SEQ ID NO: 1 and fragment of the instant SEQ ID NO: 2 (see cols. 49-50). Thus, the limitations of claims 1 are taught by the Suzuki et al. patent. Given that the antibody of the Suzuki et al. patent specifically recognizes the two regions claimed, the antibody would recognize at least two consecutive amino acids within the two regions, thus meeting the limitations of claim 2. Also, absent evidence to the contrary, the antibody would bind to at least one of the regions of SEQ ID NO: 1 and to at least one of the regions of SEQ ID NO: 2 recited by claim 3, thus meeting the limitations of claim 3. The patent teaches that the antibodies of the invention can be full-length, a F(ab)-fragment and a $F(ab)_2$-fragment (col.18, lines 10 and 11), thus meeting the limitations of claim 8. Moreover, given that the two regions of the β-A4 peptide are separated by at least 1 amino acid, the regions form a discontinuous or conformational epitope, thus meeting the limitations of claim 9. The patent also teaches pharmaceutical compositions (abstract), thus meeting the limitations of claims 15, 16, 29 and 30. It is

noted that claim 29 is a product-by-process claim. Given that the patent teaches the product itself, said claim is anticipated. A product made by any other process renders a product-by-process claim unpatentable. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985).

Since the patent teaches all the elements of the claims, claims 1-3, 8, 9, 15, 16, 29 and 30 are anticipated by U.S. Patent No. 5,955,317 to Suzuki et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,955,317 to Suzuki et al (citation A3 on the IDS dated 13 November 2007) in view of Knappik et al. (citation C3 on the IDS dated 20 August 2004).

The claims are drawn to a nucleic acid, vector and host cell that encode the antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/A β4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof.

The Suzuki et al. patent teaches as set forth above, but does not teach encoding nucleic acids, vectors or host cells. However, determining the amino acid sequence of the antibody and then the encoding nucleic acid is standard and known in the art as evidenced by the Knappik et al. reference (p.58, col.1). The Knappik et al. reference

teaches nucleic acid-vector-host cell expression and production of antibodies (p.58), as in the instant claims 11-14.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by combining the antibody of the Suzuki et al. patent with the disclosure of the Knappik et al. reference. The skilled artisan would have been motivated to make these modifications to express the antibody recombinantly because of the advantages of doing so, as taught by the Knappik et al. reference (entire document, e.g., p.58, col.1). The person of ordinary skill in the art would have had a reasonable expectation of success because both references teach that the products and methods would work (entire documents).

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
22 January 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646

Docket No.: F2842 US S3 (C018016/0180304)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
Michael BARDROFF *et al.*	)	Examiner: G. S. Emch
Serial No.: 10/505,313	)	Art Unit: 1649
Filed: August 20, 2004	)	
For: **ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE**	)	

New York, New York
June 30, 2008

RESPONSE TO OFFICE ACTION, INCLUDING AMENDMENT AND REQUEST FOR EXTENSION OF TIME

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is in response to the Non-Final Office Action mailed January 28, 2008, which set a three-month shortened statutory period for response. A two-month extension of time to respond to the Office Action is hereby requested. Accordingly, this response is filed timely upon mailing, with an executed certificate of mailing, on or before June 30, 2008, as June 28th falls on a Saturday. 37 CFR §§ 1.7, 1.8 and 1.136. Enclosed is a check in the amount of $460.00 to cover the fee for the extension of time. 37 CFR § 1.17. Please charge any required extension-of-time fees, or any other fees, not otherwise paid by check to Deposit Account No. 02-4467. A duplicate copy of this sheet is enclosed.

Please amend the application as follows:

AMENDMENTS TO THE SPECIFICATION begins on page 3 of this paper.

AMENDMENTS TO THE CLAIMS are reflected in the listing of claims, which begins on page 10 of this paper.

REMARKS begin on page 16 of this paper.

IN THE SPECIFICATION

Please delete paragraph 17 and replace with the following:

[0017] The term "two regions of the β-A4 peptide" relates to two regions as defined by their amino acid sequences shown in SEQ ID NOs: 1 and 2, relating to the N-terminal amino acids 2 to 10 and to the central amino acids 12 to 25 of β-A4 peptide. The term " β-A4 peptide" in context of this invention relates to the herein above described Aβ39, Aβ41, Aβ43, preferably to Aβ40 and Aβ42. Aβ42 is also depicted in appended SEQ ID NO: 27. It is of note that the term "two regions of the β-A4 peptide" also relates to an "epitope" and/or an "antigenic determinant" which comprises the herein defined two regions of the β-A4 peptide or parts thereof. In accordance with this invention, said two regions of the β-A4 peptide are separated (on the level of the amino acid sequence) in the primary structure of the β-A4 peptide by at least one amino acid, preferably by at least two amino acids, more preferably by at least three amino acids, more preferably by at least four amino acids, more preferably by at least five amino acids, more preferably at least six amino acids, more preferably at least nine amino acids and most preferably at least twelve amino acids. As shown herein and as documented in the appended examples, the inventive antibodies/antibody molecules detect/interact with and/or bind to two regions of the β-A4 peptide as defined herein, whereby said two regions are separated (on the primary structure level of the amino acid sequence) by at least one amino acid

and wherein the sequence separating said two regions/"epitope" may comprise more then ten amino acids, preferably 14 amino acids, more preferably 15 amino acids or 16 amino acids. For example, MSR-3 Fab (as an inventive antibody molecule) recognizes detects/interacts with two regions on the β-A4 peptide, wherein said first region comprises amino acids 3 and 4 (EF) and said second regions comprises amino acids 18 to 23 (VFFAED, SEQ ID NO: 421). Accordingly, the separating sequence between the region/epitopes to be detected/recognized has a length of 13 amino acids on the primary amino acid sequence structure. Similarly, MSR #3.4H7 IgG1, an optimized and matured antibody molecules derived from MSR-3 and comprised in an IgG1-framework, detects/interacts with/binds to two epitopes/regions of β-A4 which comprise in the first region positions 1 to 4 (DAEF) and in the second region positions 19 to 24 (FFAEDV, SEQ ID NO: 423) of β-A4 as defined herein. Accordingly, MSR #3.4H7 IgG1 recognizes/detects/interacts with/binds to two epitopes/regions which are, on the primary amino acid sequence level, separated by 14 amino acids. As detailed in the appended examples, affinity maturation and conversion of monovalent inventive Fab fragments to full-length IgG1 antibodies may result in a certain broadening of the epitopes/regions detected in pepspot, ELISA assays and the like. Therefore, the antibody molecules of the invention are capable of simultaneously and independently recognizing two regions of the β-A4 peptide/Aβ4 wherein said regions comprise the amino acid sequence as

shown in SEQ ID NO: 1 (or parts thereof) and the amino acid sequence as shown in SEQ ID NO: 2 (or (a) part(s) thereof). Due to the potential broadening of epitopes as detailed herein it is, however, also envisaged that amino acids in close proximity to the sequences of SEQ ID NO: 1 and 2 are detected/recognized, i.e. that additional amino acids are part of the two regions to be detected/recognized. Accordingly, it is also envisaged that, e.g. the first amino acid of Aβ (1-42) as defined herein, namely D (Aspartic acid) in part of one epitope to be detected/recognized or that amino acids located after the region of Aβ (1-42) as defined in SEQ ID NO: 2 are detected/recognized. Said additional amino acid may, e.g., be the amino acid on position 26 of SEQ ID NO: 27 (βA4/Aβ (1-42)), namely S (Serine).

Please deleted the last three sentences of paragraph 18 and replace with the following three sentences:

-- Preferred fragments or parts are in the first region/stretch of SEQ ID NO: 27 the amino acid sequences AEFRHD (SEQ ID NO: 415), EF, EFR, FR, EFRHDSG (SEQ ID NO: 416), EFRHD (SEQ ID NO: 417) or HDSG (SEQ ID NO: 418), and in the second region/stretch of SEQ ID NO: 27 the amino acid sequences HHQKL (SEQ ID NO: 419), LV, LVFFAE (SEQ ID NO: 420), VFFAED (SEQ ID NO: 421), VFFA (SEQ ID NO: 422) or FFAEDV (SEQ ID NO: 423). As mentioned above, said fragments may also comprise additional amino acids or may be parts of

the fragments defined herein. Specific examples are DAE, DAEF, FRH or RHDSG. --

Please delete paragraph 37 and replace with the following paragraph:

--[0037] In a preferred embodiment, the antibody molecule of the invention recognizes at least two consecutive amino acids within the two regions of Aβ4 defined herein, more preferably said antibody molecule recognizes in the first region an amino acid sequence comprising the amino acids: AEFRHD (SEQ ID NO: 415), EF, EFR, FR, EFRHDSG (SEQ ID NO: 416), EFRHD (SEQ ID NO: 417) or HDSG (SEQ ID NO: 418), and in the second region an amino acid sequence comprising the amino acids: HHQKL (SEQ ID NO: 419), LV, LVFFAE (SEQ ID NO: 420), VFFAED (SEQ ID NO: 421), VFFA (SEQ ID NO: 422) or FFAEDV (SEQ ID NO: 423). Further fragments or broadened parts comprise: DAE, DAEF, FRH or RHDSG.--

Please add the following sentence to the end of paragraph 169:

-- The V_H DNA sequence of the IgG of antibody molecule 7.9H7 after subcloning is shown in SEQ ID No.: 424, and the corresponding amino acid sequence is shown in SEQ ID No: 425.

Please delete paragraph 206 and replace with the following paragraph:

-- [0206] Employing specific of the above described heptapeptides derived from Aβ, specific ELISA-tests as described herein above were carried out. Preferably, inventive antibodies comprise antibodies which show, as measured by of optical densities, a signal to background ratio above "10" when their reactivity with an A-beta derived peptide (AEFRHD, SEQ ID NO: 415; amino acid 2 to 7 of A-beta) is compared to an non-related protein/peptide like BSA. Most preferably, the ratio of optical densities is above "5" for a corresponding reaction with at least one of the following three Aβ derived peptides: (VFFAED, SEQ ID NO: 421; amino acid 18 to 23 of Aβ) or (FFAEDV, SEQ ID NO: 423; amino acid 19 to 24 of Aβ) or (LVFFAE, SEQ ID NO: 420; amino acid 17 to 22 of Aβ). --

Please delete the first row of Table 6 and replace with the following language:

--Reactivity of MS-R Fabs with BSA-conjugated Abeta heptapeptides 2-7 (AEFRHD, SEQ ID NO: 415), 17-22 (LVFFAE, SEQ ID NO: 420), 18-23 (VFFAED, SEQ ID NO: 421) and 19-24 (FFAEDV, SEQ ID NO: 423). The ratios of the ELISA read-out (optical density) obtained with peptide-conjugated and non-conjugated BSA are given. The signal intensities obtained with the 17-22, 18-23 and 19-24 peptides in relation to the 2-7 peptide are also indicated. --

Please delete paragraph 208 and replace with the following paragraph:

-- [0208] Table 6: Reactivity of MS-R Fabs with BSA-conjugated Abeta heptapeptides 2-7 (AEFRHD, SEQ ID NO: 415), 17-22 (LVFFAE, SEQ ID NO: 420), 18-23 (VFFAED, SEQ ID NO: 421) and 19-24 (FFAEDV, SEQ ID NO: 423). The ratios of the ELISA read-out (optical density) obtained with peptide-conjugated and non-conjugated BSA are given. The signal intensities obtained with the 17-22, 18-23 and 19-24 peptides in relation to the 2-7 peptide are also indicated. --

Please delete paragraph 209 and replace with the following paragraph:

-- [0209] Table 7: Reactivity of MS-R IgGs and mouse monoclonal antibodies BAP-1, BAP-2, 4G8, 6E10 Amy-33 and 6F/3D with BSA-conjugated Aβ heptapeptides 2-7 (AEFRHD, SEQ ID NO: 415), 17-22 (LVFFAE, SEQ ID NO: 420), 18-23 (VFFAED, SEQ ID NO: 421) and 19-24 (FFAEDV, SEQ ID NO: 423). The ratios of the ELISA read-out (optical density) obtained with peptide-conjugated and non-conjugated BSA are given. The signal intensities obtained with the 17-22, 18-23 and 19-24 peptides in relation to the 2-7 peptide are also indicated. *this antibody is specific for sequence 8-17 and does not recognize N-terminal or middle epitope sequences. --

In Column 2, Row 1 of Table 7, please insert "(SEQ ID NO: 415)" after "AEFRHD." In Column 3, Row 1 of Table 7, please insert "(SEQ ID NO: 420)" after "LVFFAE." In Column 4, Row 1 of Table 7, please insert "(SEQ ID NO: 421)" after "VFFAED". In Column 5, Row 1 of Table 7, please insert "(SEQ ID NO: 423)" after "FFAEDV".

Please cancel the Sequence Listing as filed in the original application.

Please enter the Substitute Sequence Listing set forth in Exhibit 1 on the next page after the Abstract.

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

LISTING OF CLAIMS:

Claim 1. (Currently Amended) An antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/Aβ4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof, wherein said antibody molecule comprises

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 96, 130-133, 141-143, 160, 175-177, 180, 189, 190, 200, 201, 206-211, and 224;

(2) L-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 97, 144, 161, and 212; and

(3) L-CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 16, 18, 20, 75, 77, 79, 81, 83, 85, 87, 95, 98, 102, 103-107, 145, 149-159; 162, 166, 178, 183, 202, 213, 217, 218, 220, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411 and 413; and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 99, 146, 163, 203, and 214;

(2) H-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 100, 108-129, 134-140, 147, 164, 167-174, 179, 181, 182, 184-188, 191-199, 204, 205, 215, 219, and 221-223; and

(3) H-CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 22, 24, 26, 61, 63, 65, 67, 69, 71, 73, 93, 101, 148, 165, 216, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, and 383.

Claim 2. (Original) The antibody molecule of claim 1, wherein said antibody molecule recognizes at least two consecutive amino acids within the two regions of β-A4.

Claim 3. (Currently Amended) The antibody molecule of claim 1, wherein said antibody molecule recognizes in the first region an amino acid sequence ~~comprising:~~ selected from the group consisting of ~~AEFRHD~~, EF, EFR, FR, ~~EFRHDSG, EFRHD or HDSG~~ and SEQ ID NOs: 415 – 418, and in the second region an amino acid sequence ~~comprising:~~ selected from the group consisting of ~~HHQKL~~, LV, ~~LVFFAE, VFFAED, VFFA or FFAEDV~~ and SEQ ID NOs: 419 - 423.

Claim 4. (Previously presented) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_H-region as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of

SEQ ID NOs: 3, 5 and 7, or a variable V_H-region as shown in a SEQ ID NO: selected from the group consisting of SEQ ID NOs: 4, 6 and 8.

Claim 5. (Previously presented) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_L-region as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 9, 11 and 13, or a variable V_L-region as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 10, 12 and 14.

Claim 6. (Currently Amended) The antibody molecule of claim 1, wherein said antibody molecule comprises at least one CDR3 amino acid sequence of an V_L-region as encoded by a nucleic acid molecule as shown in SEQ ID NOs: 15, 17 or 19, or at least one CDR3 amino acid sequence of an V_L-region as shown in SEQ ID NOs: 16, 18 or 20; and/or wherein said antibody molecule comprises at least one CDR3 amino acid sequence of an V_H-region as encoded by a nucleic acid molecule as shown in SEQ ID NOs: 21, 23 or 25, or at least one CDR3 amino acid sequence of an V_H-region as shown in SEQ ID NOs: 22, 24 or 26.

Claim 7. (Previously presented) The antibody molecule of claim 1, wherein said antibody is selected from the group consisting of MSR-3, -7 and -8, and an affinity-matured version of MSR-3, -7 and -8.

Claim 8. (Previously presented) The antibody molecule of claim 1, wherein said antibody molecule is a full antibody (immunoglobulin), a F(ab)-fragment, a $F(ab)_2$-fragment, a single-chain antibody, a chimeric antibody, a CDR-grafted antibody, a bivalent antibody-construct, a synthetic antibody or a cross-cloned antibody.

Claim 9. (Previously presented) The antibody molecule of claim 1, wherein said two regions of β-A4 form a conformational epitope or a discontinuous epitope.

Claim 10. (Cancelled).

Claim 11. (Previously presented) A nucleic acid molecule encoding an antibody molecule according to claim 1.

Claim 12. (Original) A vector comprising the nucleic acid molecule of claim 11.

Claim 13. (Original) A host cell comprising the vector of claim 12.

Claim 14. (Previously presented) A method for the preparation of an antibody molecule comprising culturing the host cell of claim 13 under conditions that allow synthesis of said antibody molecule and recovering said antibody molecule from said culture.

Claim 15. (Previously presented) A pharmaceutical or diagnostic composition comprising an antibody molecule according to claim 1 and a carrier or diluent.

Claim 16. (Previously presented) The composition of claim 15, which is a pharmaceutical composition.

Claims 17-21. (Cancelled).

Claim 22. (Currently Amended) A kit comprising an antibody molecule according to claim 1, a nucleic acid molecule according to claim **[[16]]** 11, a vector according to claim **[[17]]** 12 or a host cell according to claim **[[18]]** 13, wherein the

antibody, nucleic acid, vector or host cell is contained in at least one vial, bottle, container or multicontainer unit.

Claims 23-28. (Cancelled).

Claim 29. (Previously presented) A composition comprising an antibody molecule produced by the method of claim 14.

Claim 30. (Previously presented) The composition of claim 16 further comprising a pharmaceutically acceptable carrier and/or diluent.

Claims 31-40. (Cancelled).

Claim 41. (New) An antibody molecule comprising

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises SEQ ID NO: 143;

(2) L-CDR2 comprises SEQ ID NO: 144; and

(3) L-CDR3 comprises SEQ ID NO: 95; and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises SEQ ID NO: 146;

(2) H-CDR2 comprises SEQ ID NOs: 192; and

(3) H-CDR3 comprises SEQ ID NOs: 93.

Claim 42. (New) The antibody molecule according to claim 41, wherein the antibody is of the IgG1 subtype.

Claim 43. (New) The antibody molecule according to claim 41, wherein the variable V_H-region comprises SEQ ID NO: 89; and the variable V_L-region region comprises SEQ ID NO: 91.

Claim 44. (New) The antibody molecule according to claim 43, wherein the antibody is of the IgG1 subtype.

Claim 45. (New) The antibody molecule according to claim 41, wherein the variable V_H-region comprises SEQ ID NO: 425; and the variable V_L-region region comprises SEQ ID NO: 91.

Claim 46. (New) The antibody molecule according to claim 45, wherein the antibody is of the IgG1 subtype.

Claim 47. (New) A pharmaceutical composition comprising an antibody molecule according to claim 41 and a pharmaceutically acceptable carrier or diluent.

Claim 48. (New) A pharmaceutical composition comprising an antibody molecule according to claim 44 and a pharmaceutically acceptable carrier or diluent.

Claim 49. (New) A pharmaceutical composition comprising an antibody molecule according to claim 46 and a pharmaceutically acceptable carrier or diluent.

REMARKS

Amendments to the Specification

The specification has been amended (at paragraphs 17, 18, 37, 206, 208, 209; and Tables 6 and 7) to insert parenthetical references to new SEQ ID NOs. 415-423, corresponding to sequences longer than four amino acids that were disclosed in the specification but were not previously included in the Sequence Listing. These sequences (also recited in the original claim 3) are also included in the accompanying Substitute Sequence Listing.

Support for the amendments noted above are found in original claim 3, and in the specification at, for example, paragraphs 17, 18, 37, 206, 208, and 209, as well as Tables 6 and 7. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

The specification is also amended at paragraph 169 (page 69, lines 12-18) to provide reference to new SEQ ID NOs: 424-425. Conforming additions have also been made to the accompanying Substitute Sequence Listing.

Supporting disclosure for new SEQ ID NOs 424-425 is found, e.g., in paragraph 169. As described in paragraph 169, after sub-cloning from Fab into IgG, the nucleic acid sequence of the V_H chains (including that of SEQ ID NO: 88, which encodes SEQ ID NO: 89) changed from "c/aattg" to "g/aattg," resulting in an amino acid change from Q to E. These changes in nucleic acid and amino acid sequence are reflected in SEQ ID NOs: 424-425. The difference between SEQ ID NO: 424 and SEQ ID NO: 88 is a single nucleotide: the seventh nucleotide of SEQ ID NO: 88 is "c," whereas the seventh nucleotide of SEQ ID NO: 88 is "g." Similarly, SEQ ID NO: 425

differs from SEQ ID NO: 89 in that the third amino acid of SEQ ID NO: 89, "Q," has been changed to "E."

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments are respectfully solicited.

Amendments to the Claims

Claim 1 has been amended to recite that the antibody molecules have specific V_L and V_H structures, based upon the various sequences comprising the six CDRs of the antibodies. Support for this amendment may be found in the specification at, for example, page 15, lines 3-15; page 16, lines 18-29; page 17, lines 3-8 and lines 25-31; page 18, lines 16-19; page 19, lines 1-5, lines 8-13, and lines 22-31; page 20, lines 1-18; Table 1 (pages 64-68); Example 13 (pages 87-95); and the Substitute Sequence Listing. The Examiner will note that the SEQ ID NOs recited in claim 1 correspond to the amino acid sequences listed in Table 1.

Claim 3 has been amended to recite "SEQ ID NOs: 415 – 418" and "SEQ ID NOs: 419 – 423," the nine SEQ ID NOs that correspond to peptide residues previously described by single letter amino acid designations. Support for this amendment may be found in the original claim 3, the specification (and as amended) at, for example, paragraphs 18 and 37, and the Substitute Sequence Listing. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claim 6 has been amended to recite "...CDR3 amino acid sequence" in two instances to parallel the other recitations of "CDR3 amino acid sequence" in the same claim. Support for this amendment may be found in the original claim 6. (*Id.*)

Claim 22 has been amended to recite "[a] kit comprising an antibody molecule according to claim 1, a nucleic acid molecule according to claim 11, a vector according to claim 12 or a host cell according to claim 13..." Support for this amendment may be found in the specification at, for example, paragraph 88.

Claim 28 has been cancelled, without prejudice.

Claims 41-49 have been added. These claims are directed to particular antibodies defined respectively by the sequences comprising their six CDRs.

Support for claim 41 may be found in the specification at, for example, page 18, lines 4-11; page 67, line 6; and in the Sequence Listing (SEQ ID NOs: 93, 95, 143, 144, 146, and 192.) Support for claim 42 may be found in the specification at, for example, page 17, lines 3-11; and page 18, lines 17-22. Support for claim 43 may be found in the specification at, for example, page 18, lines 4-11. Support for claim 44 may be found in the specification at, for example, page 17, lines 3-11; and page 18, lines 17-22. Support for claim 45 may be found in the specification at, for example, paragraph 169 (page 69, lines 12-18 as filed; and as amended above on page 6 of this Response), and the Substitute Sequence Listing (SEQ ID NO: 91 and 425). Support for claim 46 may be found in the specification at, for example, page 17, lines 3-11; and page 18, lines 17-22. Support for claims 47-49 may be found in the specification at, for example, page 28, lines 14-15.

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments are respectfully solicited.

Sequence Listing Objection

The Office Action indicated that the application as filed failed to comply with the sequence rules of 37 C.F.R. §§ 1.821 through 1.825, and in particular, 37 C.F.R. § 1.821(d), "which requires that reference be made to a particular sequence identifier (SEQ ID NO:) in the specification and claims at each disclosure of a sequence encompassed by the definitions set forth in 37 C.F.R. §§ 1.821(a)(1) and (a)(2)." (Paper No. 20080117 at 3). The Examiner asserted that "claim 3 and the supporting sections of the specification contain sequences, which are not properly identified." (*Id.*) The Examiner further stated that "[i]n case these sequences are new, Applicants must provide a substitute computer readable form (CRF) copy of a 'Sequence Listing' which includes all of the sequences that are present in the instant application and encompassed by these rules..." (*Id.*)

These alleged errors have been remedied by the amendments to claim 3, amendments to the specification, as well as the Substitute Sequence Listing, as set forth above in the "Amendment to the Specifications" and the "Amendments to the Claims" sections.

Accordingly, the previous Sequence Listing has been cancelled and a Substitute Sequence Listing in both hard copy and computer readable format are submitted herewith as Exhibits 1 and 2, respectively. Pursuant to 37 CFR § 1.821(f), undersigned counsel hereby represents that, upon information and belief, the content of the paper and computer readable Substitute Sequence Listings enclosed herewith are the same and that no new matter has been added.

It is believed that the amended specification, the amended claim 3, as well as the Substitute Sequence Listing and computer readable form presented herewith place the captioned application into compliance with the requirements set forth in 37 CFR § 1.821 *et seq.* Entry of the Substitute Sequence and withdrawal of the objection with respect to the Sequence Listing is respectfully solicited.

Indefinteness Rejection

Claims 22 and 28 were rejected under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Paper No. 20080117 at 9). In making the rejection, the Examiner asserted that the claims "depend from canceled claims, i.e. claims 17 and 18 and 27, respectfully." (*Id.*).

Claim 22 has been amended to depend from pending claims. Claim 28 has been cancelled.

Thus, it is respectfully submitted that the indefiniteness rejection has been rendered moot and should be withdrawn.

Enablement Rejection

a. Claims 4-6

Claims 4-6 were rejected under 35 USC §112, first paragraph, on the asserted grounds that the specification "does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims." (Paper No. 20080117 at 4).

In making the rejection, the Examiner asserted that the specification "does not reasonably provide enablement for an antibody and fragments thereof that do not contain a full set of 6 CDRs from the [V_H] and the [V_L] domains as broadly encompassed by the claims." (*Id.*) The Examiner, however, acknowledged that the specification is "enabling for antibodies or fragments thereof that comprise 6 CDRs, three from the [V_H] domain and three from the [V_L] domain, wherein the antibodies and fragments thereof bind the same antigen as claimed." (*Id.*)

As discussed above, independent claim 1 has been amended to recite the sequences of all 6 CDRs, three from the V_H domain and three from the V_L domain. Because claims 4-6 depend from claim 1, these dependent claims incorporate the limitations of claim 1. In view of the amendment and the Examiner's acknowledgment, it is respectfully submitted that the enablement rejection of claims 4-6 should be withdrawn.

b. Claim 7

Claim 7 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. (Paper No. 20080117 at 6). In making the rejection, the Examiner asserted that "[t]he invention appears to employ novel biological materials, specifically the MSR-3, MSR-7 and MSR-8 antibodies." (*Id.* at 7) The Examiner further asserted that "[s]ince the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public." (*Id.*) In addition, the Examiner asserted, "[t]he specification does not disclose a repeatable process to

obtain the biological materials and it is not apparent if the biological materials are readily available to the public." (*Id.*)

For reasons set forth below, the rejection is respectfully traversed.

The specification sets forth the amino acid sequences (and encoding nucleic acid sequences) of the variable regions of MSR-3, MSR-7, and MSR-8 antibodies. For example, page 14, lines 16-20 and lines 24-27 disclose the following:

> The sequences as shown in SEQ ID NOs: 3 and 4 depict the coding region and the amino acid sequence, respectively, of the V_H-region of the inventive, parental antibody MSR-3 (MS-Roche 3), the sequences in SEQ ID NOs: 5 and 6 depict the coding region and the amino acid sequence, respectively, of the V_H-region of the inventive, parental antibody MSR-7 (MS-Roche 7) and SEQ ID NOs: 7 and 8 depict the coding region and the amino acid sequence, respectively, of the V_H-region of the inventive, parental antibody MSR-8 (MS-Roche 8)... SEQ ID NOs: 9 and 10 correspond to the V_L-region of MSR-3, SEQ ID NOs: 11 and 12 correspond to the V_L-region of MSR-7 and SEQ ID NOs: 13 and 14 correspond to the V_L-region of MSR-8.

With the disclosure of both the amino acid and the encoding nucleic acid sequences, a person skilled in the art may readily construct the MSR-3, MSR-7, and MSR-8 antibody molecules. Furthermore, the six CDRs of affinity-matured versions of the antibodies are disclosed, for example, in Table 1. Thus, affinity-matured versions may also be readily reproduced. Accordingly, the specification disclose repeatable processes for obtaining the biological material as set forth in claim 7.

For the above reasons, it is respectfully submitted that the enablement rejection of claim 7 should be withdrawn.

Anticipation Rejection

Claims 1-3, 8, 9, 15, 16, 29 and 30 were rejected under 35 U.S.C. 102(b) as anticipated by Suzuki *et al.*, U.S. Patent No. 5,955,317 ("Suzuki"). (Paper No. 20080117 at 9).

In making the rejection, the Examiner asserted that Suzuki discloses "a monoclonal antibody that specifically recognizes two regions of the β-amyloid (i.e., β -A4) peptide, wherein the two regions are the amino acid sequences of SEQ ID NO: 7 and SEQ ID NO: 10." (Paper No. 20080117 at 10). The Examiner further asserted that "Suzuki['s] SEQ ID NO: 7 is the amino acid sequence DAEFRHDSGYEVHHQKLVFFAEDVGSNK, which comprises both the instant SEQ ID NO: 1 and the instant SEQ ID NO: 2..., and the Suzuki['s] SEQ ID NO: 10 is the amino acid sequence DAEFRHDSGYEVHHQK, which comprises the instant SEQ ID NO: 1 and [a] fragment of the instant SEQ ID NO: 2 (see cols. 49-50)." (*Id.*) The Examiner then contended that "[t]hus, the limitations of claims 1 are taught by the Suzuki." (*Id.*)

Reconsideration and withdrawal of the rejection is respectfully requested.

As is well settled, anticipation requires "identity of invention." *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply,* 33 USPQ2d 1496, 1498 (Fed. Cir. 1995). Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim. *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.,* 221 USPQ 481, 485 (Fed. Cir 1984).

First, it is respectfully submitted that the Examiner has misinterpreted the Suzuki reference. In particular, Suzuki does not disclose any antibody which recognizes any two nonoverlapping regions of amyloid beta 1-42, much less the two specific nonoverlapping regions recited in claim 1. To the contrary, Suzuki distinguishes antibodies based on their respective abilities to bind/not bind to unspecified amino acids contained within overlapping peptide residues, such as amino acids 1-28 (the Suzuki SEQ ID NO: 7 mentioned by the Examiner) and amino acids 1-16 (the Suzuki SEQ ID NO: 10 mentioned by the Examiner). Thus, Suzuki does not identically describe the antibodies recited in claim 1.

Moreover, claim 1 has been amended to recite that the antibody comprises six CDRs having specific amino acid sequences. By contrast, Suzuki does not describe the antibody sequence of any CDR, much less the sequences of all six CDRs of any antibody. Thus, Suzuki cannot anticipate claims 1 as amended.

Because claims 2-3, 8, 9, 15, 16, 29, and 30 depend from claim 1, they incorporate the language of claim 1 and thus are distinguishable from Suzuki for the same reasons as discussed above.

Accordingly, it is respectfully submitted that the anticipation rejection has been rendered moot and should be withdrawn.

Obviousness Rejection

Claims 11-14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki in view of Knappik *et al.*, "Fully synthetic Human Combinatorial Antibody Libraries (HuCAL) Based on Modular Consensus

Frameworks and CDRs Randomized with Trinucleotide," *J. Mol. Biol.* 296: 57-86 (2000) ("Knappik"). (Paper No. 20080117 at 12).

In making the rejection, the Examiner acknowledged that Suzuki "does not disclose encoding nucleic acids, vectors or host cells." (*Id.*) To fill the knowledge gap, the Examiner relied on Knappik and asserted that "determining the amino acid sequence of the antibody and then the encoding nucleic acid is standard and known in the art as evidenced by [] Knappik... (p.58, col.1)." (*Id.*)

The obviousness rejection is respectfully traversed.

Obviousness **must** be based upon facts, "cold hard facts." *In re Freed*, 165 USPQ 570, 571-72 (CCPA 1970). When a conclusion of obviousness is not based upon facts, it cannot stand. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (BPAI 1993).

The rejection of claims 11-14 rests upon an unsupported conclusion that some amino acid sequences not identified by the Examiner, and indeed not described in Suzuki, are "obvious". From that platform, the Examiner then concludes that the particular nucleic acid sequences recited in claims 11-14 are obvious. The rejection is thus not based on facts, as is required.

Further, claims 11-14 incorporate the functional and structural limitation recited in amended claim 1, and thus the nucleic acid molecule recited in these claims encodes or produces antibodies having six CDR regions comprising specific amino acid sequences. Suzuki's antibodies are different functionally and structurally, and their encoding nucleotides are different from and not suggestive of the nucleic acids of claims 11-14.

Knappik does not fill the factual gaps left by Suzuki. Hence, the proposed combination of Suzuki and Knappik do not disclose or suggest claims 11-14.

Accordingly, for the reasons set forth above, entry of the amendments and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on June 30, 2008.

Jihong Zang, Reg. No. 56,606

Respectfully submitted,

By: _____

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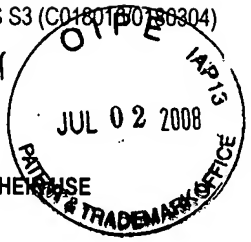
June 30, 2008 Docket No.: F2842 US S3 (C0180/B0180304)

0180304



In re Patent Application of :
Michael BARDROFF *et al.*
Serial No.: 10/505,313
Filed: August 20, 2004
For: **ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE**

Enclosed:

1. Response To Office Action Including Amendment and Request For Extension of Time with certificate of mailing (27 pp, incl. duplicate pg. 1); with Exhibits 1 & 2
   - Exhibit 1: Substitute Sequence List (200 pages)
   - Exhibit 2: Substitute Sequence List in CRF (1 diskette)
2. $460.00 check to cover two-month extension; and
3. Return Postcard

PLEASE DATE STAMP AND RETURN TO ACKNOWLEDGE RECEIPT

LZang:mh

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,313	03/07/2005	Michael Bardroff	F2842 US S3 (C018016/0180	1924

7590 07/28/2008

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
07/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Interview Summary	Application No.	Applicant(s)	
	10/505,313	BARDROFF ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Gregory S. Emch*.

(2) *Elizabeth Kemmerer*.

(3)*Stephen Haracz*.

(4)*Jihong Zang*.

Date of Interview: *09 July 2008*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: *1-9,11-16,22,29,30 and 41-49*.

Identification of prior art discussed: *None*.

Agreement with respect to the claims f)☐ was reached. g)☒ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Participants discussed the claim amendments submitted in the reply filed on 02 July 2008. The examiners informed applicants' respresentatives that it is unclear how the newly submitted claim amendments read on the elected invention. It was proposed that Applicants' representatives submit a subsequent response to address this issue. Participants also discussed the rejection of claim 7 under 35 U.S.C.112, first paragraph*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

/Gregory S. Emch/
Examiner's signature, if required

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Docket No.: F2842 US S3 (C018016/0180304)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)

Michael BARDROFF *et al.*) Examiner: G. S. Emch

Serial No.: 10/505,313) Art Unit: 1649

Filed: August 20, 2004)

For: **ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE**

New York, New York
July 24, 2008

SUPPLEMENTAL RESPONSE TO OFFICE ACTION, INCLUDING SUMMARY OF EXAMINER'S INTERVIEW, AMENDMENT AND REQUEST FOR EXTENSION OF TIME

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is a supplemental response to the Non-Final Office Action mailed January 28, 2008, which set a three-month shortened statutory period for response. Accordingly, this response is filed timely upon mailing, with an executed certificate of mailing, on or before July 28, 2008, with a three-month extension. 37 CFR §§ 1.8 and 1.136.

As a two-month extension of time to respond to the Office Action was previously requested and paid for, an additional (third) month extension is hereby requested. Enclosed is a check in the amount of $590.00 ($1050 - $460 previously paid) to cover the third month. Please charge any required extension-of-time fees, or any other fees, not otherwise paid by check to Deposit Account No. 02-4467. A duplicate copy of this sheet is enclosed.

This response is filed in view of the helpful comments and suggestions offered by Examiners Emch and Kemmerer during a telephonic interview with undersigned counsel on July 8, 2008. During the interview, the Examiners noted the restriction requirement and the search requirements implicated by the previously amended claims and requested additional amendments and/or remarks to facilitate examination of the elected subject matter. The Examiners also asked for additional comments regarding how claims 41-49 read on the elected subject matter. In addition, the enablement rejection with respect to claim 7 was discussed and further comments were requested concerning applicants' position as regard to the lack of need for deposit of MSR-7.

The issues raised during the interview are addressed below via further claim amendments and additional remarks.

Please amend the application as follows:

AMENDMENTS TO THE SPECIFICATION: None.

AMENDMENTS TO THE CLAIMS are reflected in the listing of claims, which begins on page 3 of this paper.

REMARKS begin on page 9 of this paper.

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

LISTING OF CLAIMS:

Claim 1. (Currently Amended) An antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/Aβ4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof, wherein said antibody molecule comprises

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 96, 160, 175-177, 180, 189-190, 200-201, and 206-210~~96, 130-133, 141-143, 160, 175-177, 180, 189, 190, 200, 201, 206-211, and 224~~;

(2) L-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 97 and 161 ~~97, 144, 161, and 212~~; and

(3) L-CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 18, 79, 81, 95, 149, 151-156, 158-159 and 166~~16, 18, 20, 75, 77, 79, 81, 83, 85, 87, 95, 98, 102, 103-107, 145, 149-159; 162, 166, 178, 183, 202, 213, 217, 218, 220, 385, 387, 389,~~

~~391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411 and 413~~;

and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 99 and 163~~99, 146, 163, 203, and 214~~;

(2) H-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 100, 164, 167-169, 170-174, 179, 181-182, 184-188, 192-197, 199 and 204 ~~100, 108-129, 134-140, 147, 164, 167-174, 179, 181, 182, 184-188, 191-199, 204, 205, 215, 219, and 221-223~~; and

(3) H-CDR3 comprises a sequence selected from the group consisting of SEQ ID NO: 24. ~~NOs: 22, 24, 26, 61, 63, 65, 67, 69, 71, 73, 93, 101, 148, 165, 216, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, and 383.~~

Claim 2. (Original) The antibody molecule of claim 1, wherein said antibody molecule recognizes at least two consecutive amino acids within the two regions of β-A4.

Claim 3. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule recognizes in the first region an amino acid sequence selected from the group consisting of EF, EFR, FR, and SEQ ID NOs: 415 – 418, and in the second region an amino acid sequence selected from the group consisting of LV and SEQ ID NOs: 419 - 423.

Claim 4. (Currently Amended) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_H-region comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 37, 39, 41, 43, 89, and 425. ~~as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 3, 5 and 7, or a variable V_H-region as shown in a SEQ ID NO: selected from the group consisting of SEQ ID NOs: 4, 6 and 8.~~

Claim 5. (Currently Amended) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_L-region comprising a sequence selected from the group consisting of SEQ ID NOs: 12, 51, 53, 57, and 91. ~~as encoded by a nucleic acid molecule as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 9, 11 and 13, or a variable V_L-region as shown in a SEQ ID NO selected from the group consisting of SEQ ID NOs: 10, 12 and 14.~~

Claim 6. (Cancelled).

Claim 7. (Currently Amended) The antibody molecule of claim 1, wherein said antibody is selected from the group consisting of MSR-7 ~~MSR-3, 7 and 8,~~ and an affinity-matured version of MSR-7 ~~MSR-3, 7 and 8~~.

Claim 8. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule is a full antibody (immunoglobulin), a F(ab)-fragment, a $F(ab)_2$-fragment, a single-chain antibody, a chimeric antibody, a CDR-grafted antibody, a bivalent antibody-construct, a synthetic antibody or a cross-cloned antibody.

Claim 9. (Previously Presented) The antibody molecule of claim 1, wherein said two regions of β-A4 form a conformational epitope or a discontinuous epitope.

Claim 10. (Cancelled).

Claim 11. (Previously Presented) A nucleic acid molecule encoding an antibody molecule according to claim 1.

Claim 12. (Original) A vector comprising the nucleic acid molecule of claim 11.

Claim 13. (Original) A host cell comprising the vector of claim 12.

Claim 14. (Previously Presented) A method for the preparation of an antibody molecule comprising culturing the host cell of claim 13 under conditions that allow synthesis of said antibody molecule and recovering said antibody molecule from said culture.

Claim 15. (Previously Presented) A pharmaceutical or diagnostic composition comprising an antibody molecule according to claim 1 and a carrier or diluent.

Claim 16. (Previously Presented) The composition of claim 15, which is a pharmaceutical composition.

Claims 17-21. (Cancelled).

Claim 22. (Previously Presented) A kit comprising an antibody molecule according to claim 1, a nucleic acid molecule according to claim 11, a vector according to claim 12 or a host cell according to claim 13, wherein the antibody, nucleic acid, vector or host cell is contained in at least one vial, bottle, container or multicontainer unit.

Claims 23-28. (Cancelled).

Claim 29. (Previously Presented) A composition comprising an antibody molecule produced by the method of claim 14.

Claim 30. (Previously Presented) The composition of claim 16 further comprising a pharmaceutically acceptable carrier and/or diluent.

Claims 31-40. (Cancelled).

Claim 41. (Previously Presented) An antibody molecule comprising

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises SEQ ID NO: 143;

(2) L-CDR2 comprises SEQ ID NO: 144; and

(3) L-CDR3 comprises SEQ ID NO: 95; and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises SEQ ID NO: 146;

(2) H-CDR2 comprises SEQ ID NOs: 192; and

(3) H-CDR3 comprises SEQ ID NOs: 93.

Claim 42. (Previously Presented)The antibody molecule according to claim 41, wherein the antibody is of the IgG1 subtype.

Claim 43. (Previously Presented) The antibody molecule according to claim 41, wherein the variable V_H-region comprises SEQ ID NO: 89; and the variable V_L-region comprises SEQ ID NO: 91.

Claim 44. (Previously Presented) The antibody molecule according to claim 43, wherein the antibody is of the IgG1 subtype.

Claim 45. (Previously Presented) The antibody molecule according to claim 41, wherein the variable V_H-region comprises SEQ ID NO: 425; and the variable V_L-region comprises SEQ ID NO: 91.

Claim 46. (Previously Presented) The antibody molecule according to claim 45, wherein the antibody is of the IgG1 subtype.

Claim 47. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 41 and a pharmaceutically acceptable carrier or diluent.

Claim 48. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 44 and a pharmaceutically acceptable carrier or diluent.

Claim 49. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 46 and a pharmaceutically acceptable carrier or diluent.

REMARKS

Amendments to the Claims

Claim 1 has been further amended to omit subject matter related to MSR-3 and MSR-8 and to instead recite only subject matter related to MSR-7, the elected species.

In particular, claim 1 now recites that the antibody molecules comprise CDRs of the MSR-7 antibody and the affinity-matured versions thereof described in Table 1. The SEQ ID NOs recited in claim 1 correspond only to the CDR amino acid sequences of MSR-7 antibody and the affinity-matured versions thereof listed in Table 1. The portion of Table 1 listing the CDR sequences of such MSR-7 antibody and the affinity-matured versions, as well as the corresponding SEQ ID NOs. of such sequences, are shown in the attached Exhibit 1.

The Examiner will note that there is only one sequence for H-CDR3, and that there are only two sequences for each of H-CDR1 and L-CDR2. This redundancy, along with the deletion of CDR sequences relating to MSR-3 and MSR-8, should facilitate search and examination, as the Examiners requested.

Support for the amendment to claim 1 may be found in Table 1 at pages 64-68, and see also the specification at, for example, page 15, lines 3-15; page 16, lines 18-29; page 20, lines 1-18. See also the original Sequence Listing as filed; and the Substitute Sequence Listing.

Claim 4 has been amended to omit subject matter related to MSR-3 and MSR-8. As amended, claim 4 recites specific heavy chain variable sequences that include H-CDRs of MSR-7 antibody or certain affinity-matured versions thereof. The

Examiner will note that the framework regions surrounding the CDRs are included in the recited sequences. The table below sets forth the SEQ ID No. of each of the three H-CDRs contained within the variable heavy chain sequences now recited in claim 4; SEQ ID NO: 6 is the sequence for the variable heavy chain of MSR-7.

SEQ ID NO.	H-CDR1 SEQ ID NO.	H-CDR2 SEQ ID NO.	H-CDR3 SEQ ID NO.
6	99	100	24
37	99	182	24
39	99	185	24
41	99	187	24
43	99	195	24
89	99	192	24
425	99	192	24

Support for the amendment to claim 4 may be found in original claim 4 and in the specification at, for example, page 14, lines 9-30; page 18, lines 6-15; the original Sequence Listing as filed, and the Substitute Sequence Listing. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

A conforming amendment has also been made to claim 5 in order to delete subject matter related to MSR-3 and MSR-8. Claim 5 as amended recites specific light chain variable sequences that include L-CDRs of MSR-7 antibody or certain affinity-matured versions thereof. The Examiner will note that the framework regions are included in such variable light chain sequences. The table below sets forth the SEQ ID No. of each of the three L-CDRs contained within the variable light chain sequences now recited in claim 5; SEQ ID No: 12 is the sequence for the variable light of MSR-7.

SEQ ID No.	L-CDR1 SEQ ID NO.	L-CDR2 SEQ ID NO.	L-CDR3 SEQ ID NO.
12	96	97	18
51	175	97	79
53	206	161	81
57	200	97	159
91	96	97	95

Support for the amendment to claim 5 may be found in original claim 5 and in the specification at, for example, page 14, lines 9-30; page 18, lines 6-15; the original Sequence Listing as filed, and the Substitute Sequence Listing. *Id.*

Claim 7 has been amended to omit subject matter related to MSR-3 and MSR-8, reciting only the MSR-7 antibody and affinity-matured versions thereof. Support for this amendment may be found in original claim 7. *Id.*

It is submitted that no new matter has been introduced by the foregoing amendments.

Claims 41-49

With respect to the Examiners' request for supplemental comments regarding how claims 41-49 read on the elected MSR-7 species, the six CDRs recited in claim 41 are taken from the family of MSR-7 CDRs that are now recited in independent claim 1. See discussion above explaining how claim 1 has been amended to recite only CDRs of the elected MSR-7 family, omitting the MSR-3 and MSR-8 families. More particularly, claims 41-49 recite the six CDRs of "MSR-7.9 H7," a particular affinity-matured derivative of MSR-7. See Table 1 at page 67.

Claim 43 recites the complete variable heavy region (SEQ ID NO:89) and the complete variable light region (SEQ ID NO: 91) of MSR-7.9 H7. See Table 10 at

page 98. The structure embraced by claim 43 thus includes the six CDRs recited in claim 41 and also includes the adjacent framework residues contained within the specified variable regions.

As noted in the Response dated June 30, 2008, claim 45 recites the same variable light region (SEQ ID NO: 91) as claim 43, but recites a slightly different variable heavy region (SEQ ID NO: 425). As previously noted, SEQ ID NO: 425 differs from SEQ ID NO: 89 in that the third residue of SEQ ID NO: 425 is "E" rather than "Q." This difference is in the framework residues and not in any of the six CDRs commonly embraced by claims 41-49.

In summary, it is believed that claims 41-49, directed to two closely related affinity matured relatives of MSR-7, read on and are consistent with the elected subject matter. Should the Examiner's be of a different view, it is respectfully requested that the subject matter of claim 41 be treated as a single elected species for purposes of the restriction requirement and initial search and examination of the amended claims.

Enablement Rejection – Claim 7

Claim 7 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. (Paper No. 20080117 at 6). In making the rejection, the Examiner asserted that "[t]he invention appears to employ novel biological materials, specifically the MSR-3, MSR-7 and MSR-8 antibodies." (*Id.* at 7.) The Examiner further asserted that "[s]ince the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public." (*Id.*) In addition, the Examiner asserted, "[t]he specification does not disclose a repeatable process to

obtain the biological materials and it is not apparent if the biological materials are readily available to the public." (*Id.*)

The rejection is respectfully traversed. The applicants submit the following reasons in addition to the reasons set forth in the Response dated June 30, 2008.

Initially, we note that claim 7 has been amended to delete MSR-3 and MSR-8.

We also note that the Examiner has expressly acknowledged that the specification is "enabling for antibodies or fragments thereof that comprise 6 CDRs, three from the [V_H] domain and three from the [V_L] domain." (Paper No. 20080117 at 4). With regard to MSR-7, the specification lists all 6 CDRs for MSR-7 and for affinity matured versions thereof (see, *e.g.*, Table 1, pages 64-68). In view of the Examiner's acknowledgment that the disclosed CDR sequences enable one to make and use the claimed antibodies, including MSR-7, it is respectfully submitted that no deposit of MSR-7 is needed.

Indeed, Table 10 sets forth the SEQ ID NOs of amino acid sequences of the <u>full</u> variable regions of MSR-7, as well as the DNA sequence encoding such amino acid sequences (page 98). SEQ ID NOs: 5 and 6 are the encoding DNA and amino acid sequences, respectively, of the V_H-region of MSR-7. SEQ ID NOs: 11 and 12 correspond to the encoding DNA sequence and the amino acid sequences of the V_L-region of MSR-7, respectively. The variable heavy and light sequences include not only the CDRs, but also the framework amino acids surrounding the CDRs.

In view of the Examiner's acknowledgement, and in view of the reasons set forth above and in the Response dated June 30, 2008, it is respectfully submitted that the enablement rejection of claim 7 should be withdrawn. The specification describes not only the six CDRs of MSR-7, but also the amino acid sequence of the complete variable heavy and light chains of MSR-7. The specification also describes encoding DNA sequences for both the six CDRs of MSR-7 and the complete variable heavy and light chains of MSR-7.

Given the description of the complete structure, there is no need for a cell line that makes that structure. To conclude otherwise would require deposit of every specific embodiment for which CDRs and variable sequences are provided, which is not a requirement under § 112, first paragraph.

Reconsideration and withdrawal of the enablement rejection of claim 7 is respectfully requested.

For the reasons set forth above, entry of the amendments and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 24, 2008.

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Respectfully submitted,

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Name	L-CDR1	SEQ ID NO.	L-CDR2	SEQ ID NO.	L-CDR3	SEQ ID NO.	H-CDR1	SEQ ID NO.	H-CDR2	SEQ ID NO.	H-CDR3	SEQ ID NO.
MS-Roche #7	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	FQLYSDPF	18, 145	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQLYSSPY	149	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.3	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQVYSHPF	151, 178	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.4	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYNFPH	152	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.5	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQVYSSPF	153	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.6	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQLYSPPY	154	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.7	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQVYSAPF	155	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.8	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQVYSFPI	156	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.10	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQVYNPPH	158	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.11	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12	RASQYVSSPYLA	160	GSSNRAT	97, 144, 212	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	99, 146, 214	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.13	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQVYSPPF	166	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINANGLKKYYADSVKG	167	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.H2	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINGTGMKKYYADSVKG	168	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.H3	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINANGYKTYYADSVKG	169, 198	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.H4	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINSKGSRIYYADSVKG	170	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.H5	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINATGRSKYYADSVKG	171	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381

MS-Roche #7.2.H6	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINARGNRTYYADSVKG	172	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.H7	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINSRGSDTHYADSVKG	173	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.H8	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINASGHKTYYADSVKG	174	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.L1	RASQYVDRTYLA	175	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.L3	RASQYISFRYLA	176	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.2.L4	RASQFIRRSYLA	177	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.3.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	HQVYSHPF	151, 178	GFTFSSYAMS	99, 146, 214	AISAISNKTYYADSVKG	179	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.3.L1	RASQYLHYGYLA	180	GASSRAT	97, 144, 212	HQVYSHPF	151, 178	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.4.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYNFPH	152	GFTFSSYAMS	99, 146, 214	AINATGYRTYYADSVKG	181	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.4.H2	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYNFPH	152	GFTFSSYAMS	99, 146, 214	AINYNGARIYYADSVKG	182	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINANGQRKFYADSVKG	184	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H2	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINADGNRKYYADSVKG	185	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H3	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINYQGNRKYYADSVKG	186	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H4	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINAVGMKKFYADSVKG	187	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H5	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINHAGNKKYYADSVKG	188	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.L1	RASQRLSPRYLA	189	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.L 2	RASQYLHKRYLA	190	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H8	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQIYSFPH	79, 87, 150, 399, 403, 407	GFTFSSYAMS	99, 146, 214	AINARGNRTYYADSVKG	172	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H7	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINASGTRTYYADSVKG	192	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381

MS-Roche #7.9.H8	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINASGSKIYYADSVKG	193	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.9.H9	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	LQIYNMPI	95, 157, 183, 409	GFTFSSYAMS	99, 146, 214	AINGKGNKKYYADSVKG	194	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.11.H1	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GFTFSSYAMS	99, 146, 214	GINAAGFRTYYADSVKG	195	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.11.H2	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GFTFSSYAMS	99, 146, 214	AINANGYKKYYADSVKG	196	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.11.H3	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GFTFSSYAMS	99, 146, 214	GINANGNRTYYADSVKG	197	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.11.H4	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GFTFSSYAMS	99, 146, 214	AINANGYKTYYADSVKG	169, 198	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.11.H5	RASQSVSSSYLA	96, 143, 211	GASSRAT	97, 144, 212	QQVYSPPH	159	GFTFSSYAMS	99, 146, 214	AINAHGQRTYYADSVKG	199	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche # 7.11.L1	RASQRILRIYLA	200	GASSRAT	97, 144, 212	QQVYSPPH	159	GFTFSSYAMS	99, 146, 214	AISGSGGSTYYADSVKG	100, 147, 215	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.H1	RASQYVFRRYLA	201	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NINGNGNRKYYADSVKG	204	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.L1	RASQYVFRRYLA	201	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.L2	RASQRFFYKYLA	206	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.L3	RASQFVRRGFLA	207	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.L4	RASQRLKRSYLA	208	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.L5	RASQRLKRSYLA	208	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.L6	RASQYLWYRYLA	209	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381
MS-Roche #7.12.L7	RASQWIRKTYLA	210	GSSNRAT	161	LQLYNIPN	81, 83, 162, 202, 401, 405, 411	GFTFSSYGMS	163, 203	NISGSGSSTYYADSVKG	164, 205	GKGNTHKPYGYVRYFDV	24, 65, 67, 69, 71, 73, 93, 148, 165, 369, 371, 373, 375, 377, 379, 381

July 24, 2008

Docket No.: F2842 US S3 (0018015/04B0304)

In re Patent Application of :
Michael BARDROFF *et al.*
Serial No.: 10/505,313
Filed: August 20, 2004
For: **ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE**

Enclosed:

1. Supplemental Response To Office Action, Including Summary of Examiner's Interview, Amendment and Request For Extension of Time with certificate of mailing (16 pages including duplicate pg. 1) with Exhibit 1 (3 pages)
2. $590.00 check to cover extension of time fees; and
3. Return Postcard

PLEASE DATE STAMP AND RETURN TO ACKNOWLEDGE RECEIPT

JZang:mh

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,313	03/07/2005	Michael Bardroff	F2842 US S3 (C018016/0180	1924

7590 10/14/2008

Stephen M Haracz
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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
10/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10505313 (C018016/0180	3/7/2005	BARDROFF ET AL.	F2842 US S3

Stephen M Haracz
Bryan Cave
1290 Avenue of the Americas
New York, NY 10104-3300

EXAMINER	
Gregory S. Emch	
ART UNIT	**PAPER**
1649	20081009

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

Election/Restrictions

The amendment filed on 28 July 2008 canceling all claimed subject matter drawn to the elected invention and presenting only claims drawn to a non-elected invention is non-responsive (MPEP § 821.03). Applicants have already received an action on the merits for the elected species of the MSR-7 antibody. Applicants are reminded that they were required to elect one antibody species in the restriction requirement dated 05 June 2007 (note: one antibody, NOT family of antibodies). According to Applicants' specification (e.g. Figure 4 and sequence listing), the 6 CDR sequences for the elected MSR-7 antibody are L-CDR1=SEQ ID NO: 143, L-CDR2=SEQ ID NO: 144, L-CDR3=SEQ ID NO: 18, H-CDR1=SEQ ID NO: 146, H-CDR2=SEQ ID NO: 147 and H-CDR3=SEQ ID NO: 24. Thus, newly amended claim 1 and newly presented claim 41 (as of amendment dated 02 July 2008) and dependent claims are directed to an invention(s) that is independent or distinct from the invention originally claimed because none of the claims encompass the CDR sequences of the elected MSR-7 species.

Since the above-mentioned amendment appears to be a bona fide attempt to reply, applicant is given a TIME PERIOD of ONE (1) MONTH or THIRTY (30) DAYS, whichever is longer, from the mailing date of this notice within which to supply the omission or correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD UNDER 37 CFR 1.136(a) ARE AVAILABLE.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G.E./
Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
09 October 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646

PTO-90C (Rev.04-03)

Docket No.: F2842 US S3 (C018016/0180304)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
Michael BARDROFF *et al.*	)	Examiner: G. S. Emch
Serial No.: 10/505,313	)	Art Unit: 1649
Filed: August 20, 2004	)	
For: **ANTI-AMYLOID BETA ANTIBODIES AND THEIR USE**		

New York, New York
January 13, 2009

RESPONSE TO OFFICE COMMUNICATION, INCLUDING SUMMARY OF EXAMINER INTERVIEW, AND REQUEST FOR EXTENSION OF TIME

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is a response to the Office Communication mailed October 14, 2008, which set a one-month shortened statutory period for response. As requested by the Examiners, the remarks presented herein serve to memorialize the clarifications and understandings reached during the Examiner Interview conducted on December 3, 2008.

A two-month extension of time to respond to the Office Communication is hereby requested. Accordingly, this response is filed timely upon mailing, with an executed certificate of mailing, on or before January 14, 2009. 37 CFR §§ 1.8 and 1.136. Enclosed is a check in the amount of $490. 37 CFR § 1.17. Please charge any required extension-of-time fees, or any other fees, not otherwise paid by check to Deposit Account No. 02-4467. A duplicate copy of this sheet is enclosed.

Please amend the application as follows:

AMENDMENTS TO THE SPECIFICATION: None.

AMENDMENTS TO THE CLAIMS: None. List of claims begins on page 3 of this paper.

REMARKS begin on page 8 of this paper.

LISTING OF CLAIMS:

Claim 1. (Previously Presented) An antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/Aβ4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof, wherein said antibody molecule comprises

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 96, 160, 175-177, 180, 189-190, 200-201, and 206-210;

(2) L-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 97 and 161; and

(3) L-CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 18, 79, 81, 95, 149, 151-156, 158-159 and 166; and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 99 and 163;

(2) H-CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 100, 164, 167-169, 170-174, 179, 181-182, 184-188, 192-197, 199 and 204; and

(3) H-CDR3 comprises a sequence selected from the group consisting of SEQ ID NO: 24.

Claim 2. (Original) The antibody molecule of claim 1, wherein said antibody molecule recognizes at least two consecutive amino acids within the two regions of β-A4.

Claim 3. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule recognizes in the first region an amino acid sequence selected from the group consisting of EF, EFR, FR, and SEQ ID NOs: 415 – 418, and in the second region an amino acid sequence selected from the group consisting of LV and SEQ ID NOs: 419 - 423.

Claim 4. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_H-region comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 37, 39, 41, 43, 89, and 425.

Claim 5. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule comprises a variable V_L-region comprising a sequence selected from the group consisting of SEQ ID NOs: 12, 51, 53, 57, and 91.

Claim 6. (Cancelled).

Claim 7. (Previously Presented) The antibody molecule of claim 1, wherein said antibody is selected from the group consisting of MSR-7 and an affinity-matured version of MSR-7.

Claim 8. (Previously Presented) The antibody molecule of claim 1, wherein said antibody molecule is a full antibody (immunoglobulin), a F(ab)-fragment, a

$F(ab)_2$-fragment, a single-chain antibody, a chimeric antibody, a CDR-grafted antibody, a bivalent antibody-construct, a synthetic antibody or a cross-cloned antibody.

Claim 9. (Previously Presented) The antibody molecule of claim 1, wherein said two regions of β-A4 form a conformational epitope or a discontinuous epitope.

Claim 10. (Cancelled).

Claim 11. (Previously Presented) A nucleic acid molecule encoding an antibody molecule according to claim 1.

Claim 12. (Original) A vector comprising the nucleic acid molecule of claim 11.

Claim 13. (Original) A host cell comprising the vector of claim 12.

Claim 14. (Previously Presented) A method for the preparation of an antibody molecule comprising culturing the host cell of claim 13 under conditions that allow synthesis of said antibody molecule and recovering said antibody molecule from said culture.

Claim 15. (Previously Presented) A pharmaceutical or diagnostic composition comprising an antibody molecule according to claim 1 and a carrier or diluent.

Claim 16. (Previously Presented) The composition of claim 15, which is a pharmaceutical composition.

Claims 17-21. (Cancelled).

Claim 22. (Previously Presented) A kit comprising an antibody molecule according to claim 1, a nucleic acid molecule according to claim 11, a vector according

to claim 12 or a host cell according to claim 13, wherein the antibody, nucleic acid, vector or host cell is contained in at least one vial, bottle, container or multicontainer unit.

Claims 23-28. (Cancelled).

Claim 29. (Previously Presented) A composition comprising an antibody molecule produced by the method of claim 14.

Claim 30. (Previously Presented) The composition of claim 16 further comprising a pharmaceutically acceptable carrier and/or diluent.

Claims 31-40. (Cancelled).

Claim 41. (Previously Presented) An antibody molecule comprising

(a) a variable V_L-Region comprising complementary determining regions, L-CDR1, L-CDR2, L-CDR3, wherein:

(1) L-CDR1 comprises SEQ ID NO: 143;

(2) L-CDR2 comprises SEQ ID NO: 144; and

(3) L-CDR3 comprises SEQ ID NO: 95; and

(b) a variable V_H-Region comprising complementary determining regions, H-CDR1, H-CDR2, H-CDR3, wherein:

(1) H-CDR1 comprises SEQ ID NO: 146;

(2) H-CDR2 comprises SEQ ID NOs: 192; and

(3) H-CDR3 comprises SEQ ID NOs: 93.

Claim 42. (Previously Presented)The antibody molecule according to claim 41, wherein the antibody is of the IgG1 subtype.

Claim 43. (Previously Presented) The antibody molecule according to claim 41, wherein the variable V_H-region comprises SEQ ID NO: 89; and the variable V_L-region comprises SEQ ID NO: 91.

Claim 44. (Previously Presented) The antibody molecule according to claim 43, wherein the antibody is of the IgG1 subtype.

Claim 45. (Previously Presented) The antibody molecule according to claim 41, wherein the variable V_H-region comprises SEQ ID NO: 425; and the variable V_L-region comprises SEQ ID NO: 91.

Claim 46. (Previously Presented) The antibody molecule according to claim 45, wherein the antibody is of the IgG1 subtype.

Claim 47. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 41 and a pharmaceutically acceptable carrier or diluent.

Claim 48. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 44 and a pharmaceutically acceptable carrier or diluent.

Claim 49. (Previously Presented) A pharmaceutical composition comprising an antibody molecule according to claim 46 and a pharmaceutically acceptable carrier or diluent.

REMARKS

Summary of Office Communication and Examiner Interview

In the Office Communication dated October 14, 2008, the Examiner asserted that "[t]he amendment filed on 28 July 2008 canceling all claimed subject matter drawn to the elected invention and presenting only claims drawn to a non-elected invention is non-responsive." (Paper 20081009 at 1). The Examiner further asserted that "[a]ccording to Applicants' specification (e.g. Figure 4 and sequence listing), the 6 CDR sequences for the elected MSR-7 antibody are L-CDR1=SEQ ID NO: 143, L-CDR2=SEQ ID NO: 144, L-CDR3=SEQ ID NO: 18, H-CDR1=SEQ ID NO: 146, H-CDR2=SEQ ID NO: 147 and H-CDR3=SEQ ID NO: 24." (*Id.*) The Examiner concluded, "[t]hus, newly amended claim 1 and newly presented claim 41 (as of amendment dated 02 July 2008 [sic]) and dependent claims are directed to an invention(s) that is independent or distinct from the invention originally claimed because none of the claims encompass the CDR sequences of the elected MSR-7 species." (*Id.*)

On December 3, 2008, a telephonic Examiner's Interview was conducted between Stephen Haracz and Jihong Zang, Applicants' attorneys, and Examiners Emch and Kemmerer. The purpose of the interview was to clarify for the Examiners that the amended claims are drawn to the elected invention and thus are responsive. We thank the Examiners for their participation and stated understanding of the explanation. During the Interview, issues raised in the Office Communication dated October 14, 2008 were discussed. As requested by the Examiners, the explanations are hereby memorialized and set forth below.

The amended claims encompass the CDR sequences of MSR-7

As explained during the interview, amended claim 1 recites the six CDR sequences of MSR-7 antibody; the confusion is due to the fact that the SEQ ID NOs. recited in claim 1 are different from those noted by the Examiner. The sequence listing contains redundant SEQ ID NOs. for the same sequence. In an effort to simplify the claim, we omitted the redundant SEQ ID NOs., including, unfortunately, the particular SEQ ID NOs. recited by the Examiner in the Office Communication. However, the SEQ ID NOs. of the MSR-7 CDRs referenced by the Examiner set forth the same amino acids as the SEQ ID NOs. listed in claim 1, as shown in the chart below.

	SEQ ID NO. cited by the Examiner	Corresponding SEQ ID NO. listed in Claim 1	Sequence
L-CDR1	143	96	RASQSVSSSYLA
L-CDR2	144	97	GASSRAT
L-CDR3	18	18	FQLYSDPF
H-CDR1	146	99	GFTFSSYAMS
H-CDR2	147	100	AISGSGGSTYYADSVKG
H-CDR3	24	24	GKGNTHKPYGYVRYFDV

For a complete listing of the redundant SEQ ID NOs, the Examiner is referred to the chart submitted as Exhibit 1 of the Response mailed on July 24, 2008. The chart shows the sequences of the CDRs in columns 2, 4, 6, 8, 10, and 12 as well as the corresponding SEQ ID NOs. in columns 3, 5, 7, 9, 11, and 13.

In summary, the amino acid sequences of the six CDRs of MSR-7 are recited in claim 1, and they have already been searched and examined as stated in the

Office Communication. (Paper 20081009 at 1). Because the SEQ ID NOs. of the CDRs of the elected MSR-7 antibody are included in the amended claim 1, it is respectfully submitted that the Response mailed on July 24, 2008 is responsive.

Claims 41-49 closely correspond to the subject matter already searched

As we explained and as the Examiners acknowledged during the interview, the restriction requirement was understood to embrace a family of MSR-7 antibodies rather than a single parental antibody. Claim 41 was presented because MSR7.9.H.7 is an affinity matured version of MSR-7, having substantial structural identity to MSR-7.

Because MSR7.9.H.7 derives from MSR-7, the CDR sequences of the two antibodies are very similar. In fact, four of the six CDR sequences of MSR7.9.H.7 (L-CDR1, L-CDR2, H-CDR1, and H-CDR3) are identical to that of MSR-7 antibody, which has already been searched. The sequences of the two related antibodies are further compared in the chart below.

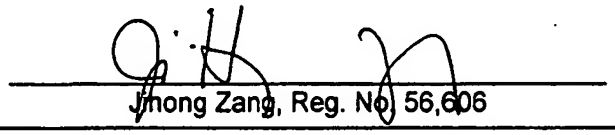
	MSR-7	MSR7.9.H.7
L-CDR1	RASQSVSSSYLA	same
L-CDR2	GASSRAT	same
L-CDR3	FQLYSDPF	LQIYNMPI
H-CDR1	GFTFSSYAMS	same
H-CDR2	AISGSGGSTYYADSVKG	AINASGTRTYYADSVKG
H-CDR3	GKGNTHKPYGYVRYFDV	same

As shown above, the similarity between MSR-7 and MSR7.9.H.7 goes beyond the 4 identical CDR sequences. A fifth CDR, H-CDR2, shares 13 of 17 residues (consensus sequence: AIXXSGXXTYYADSVKG).

Thus, four of the six CDR sequences recited in claims 41-49 have already been searched and examined on the merits. Further searches are not believed necessary to continue with claims 41-49. Therefore, we respectfully request that claims 41-49, which list the CDRs of MSR7.9.H.7, be considered because they closely correspond to the MSR-7, whose CDR sequences have already been searched and examined.

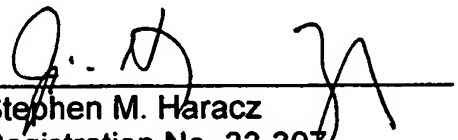
For the reasons set forth above, examination and allowance of the amended claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on January 13, 2009.



Jihong Zang, Reg. No. 56,606

Respectfully submitted,

By: 

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January 13, 2009 Docket No.: F2842 US S3 (C018016/0180304)

In re Patent Application of :
Michael BARDROFF *et al.*
Serial No.: 10/505,313
Filed: August 20, 2004
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Enclosed:

1. Response To Office Communication, Including Summary of Examiner Interview, and Request For Extension of Time with certificate of mailing (12 pages including duplicate pg. 1)
2. $490.00 check to cover extension of time fees; and
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JZang:mh

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,313	BARDROFF ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/02/08, 07/28/08 and 01/16/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-9,11-16,22,29,30 and 41-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *41-44 and 46-49* is/are allowed.

6)☒ Claim(s) *1-5,7-9,11-16,22,29 and 30* is/are rejected.

7)☒ Claim(s) *1-5,7-9,11-16,22,29,30 and 45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/21/09*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20090422*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claims 1, 3, 6 and 22 have been amended, claim 28 has been canceled and new claims 41-49 have been added as requested in the amendment filed on 02 July 2008. Claims 1, 4, 5 and 7 have been amended, and claim 6 has been canceled as requested in the amendment filed on 28 July 2008. Further, the response filed on 16 January 2009 has been received and entered in full. No claim amendments were submitted in the response filed on 16 January 2009.

As stated in the notice of non-responsive amendment dated 14 October 2008, applicants have elected one antibody species, i.e. the MSR-7 antibody, from the species set forth in the restriction requirement dated 05 June 2007. According to the specification (e.g. Figure 4 and sequence listing), the 6 CDR sequences for the elected MSR-7 antibody are L-CDR1=SEQ ID NO: 143, L-CDR2=SEQ ID NO: 144, L-CDR3=SEQ ID NO: 18, H-CDR1=SEQ ID NO: 146, H-CDR2=SEQ ID NO: 147 and H-CDR3=SEQ ID NO: 24. Thus, the amendment dated 02 July 2008 presented claims that were considered non-elected because claim 1 and dependent claims recite different sequences from those set forth above. In the response filed on 16 January 2009 (see pp.9-11), applicants assert that the amended claims still encompass the CDR sequences of MSR-7. Applicants assert that the sequence listing contains redundant SEQ ID NOs for the same sequence and assert that L-CDR1=SEQ ID NO: 143 is the same as SEQ ID NO: 96, L-CDR2=SEQ ID NO: 144 is the same as SEQ ID NO: 97, H-

CDR1=SEQ ID NO: 146 is the same as SEQ ID NO: 99 and H-CDR2=SEQ ID NO: 147 is the same as SEQ ID NO: 100. Applicants also assert that claim 41 was presented because MSR7.9.H.7 is an affinity matured version of MSR-7, having substantial structural identity to MSR-7. Applicants assert that four of the six CDR sequences of MSR7.9.H.7 (L-CDR1, L-CDR2, H-CDR1, and H-CDR3) are identical to that of MSR-7 antibody, which has already been searched. Applicants request that claims 41-49, which list the CDRs of MSR7.9.H.7, be considered because they closely correspond to the MSR-7, whose CDR sequences have already been searched and examined.

Applicants' arguments have been fully considered and are found persuasive. The examiner agrees that claim 1 and dependent claims still encompass the elected antibody of MSR-7 (note: L-CDR1=SEQ ID NO: 96, L-CDR2=SEQ ID NO: 97, L-CDR3=18, H-CDR1=SEQ ID NO: 99, H-CDR2=SEQ ID NO: 100, and H-CDR3=SEQ ID NO: 24). The two additional sequences of MSR7.9.H.7 recited by claim 41 and dependent claims, i.e. SEQ ID NO: 95 and SEQ ID NO: 93 will also be examined.

Claims 1-5, 7-9, 11-16, 22, 29, 30 and 41-49 are now pending and under consideration to the extent that the claims encompass the 8 CDR sequences set forth above (for search purposes).

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed on 21 January 2009 is enclosed in this action. One reference was crossed out because it was not

furnished in English and there was no statement of the relevance of the reference in compliance with the requirements of 37 CFR1.98 (a)(3). See MPEP 609. Although applicants have stated they have provided a concise explanation of the relevance of the document, the examiner is unable to find any such explanation.

Objections/Rejections Withdrawn

The Sequence Rules Requirement set forth in the previous office action dated 28 January 2008 is withdrawn in response to submission of the amended sequence listing and the amendments to the specification.

The rejection of claims 1-3, 8, 9, 15, 16, 29 and 30 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,955,317 to Suzuki et al. is withdrawn in response to the amendment to the claims to recite 6 specific CDR sequences, which are not disclosed by Suzuki et al.

The rejection of claims 11-14 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,955,317 to Suzuki et al. in view of Knappik et al. is withdrawn in response to the amendment to the claims to recite 6 specific CDR sequences, which are not disclosed by Suzuki et al. or Knappik et al.

The scope of enablement rejection of claims 4 and 5 under 35 U.S.C. 112, first paragraph, is withdrawn in response to the amendment to the claims to recite 6 specific CDR sequences.

The scope of enablement rejection of claim 6 under 35 U.S.C. 112, first paragraph, is withdrawn as moot in response to the cancellation of said claim.

The rejection of claim 22 under 35 U.S.C. 112, second paragraph, is withdrawn in response to the amendment to the claim that deleted dependency on canceled claims.

The rejection of claim 28 under 35 U.S.C. 112, second paragraph, is withdrawn as moot in response to the cancellation of said claim.

New and remaining issues are set forth below.

Claim Objections

Claims 1-5, 7-9, 11-16, 22, 29 and 30 are objected to because of the following informalities: The claims contain non-elected subject matter (SEQ ID NOs other than L-CDR1=SEQ ID NO: 96, L-CDR2=SEQ ID NO: 97, L-CDR3=18, H-CDR1=SEQ ID NO: 99, H-CDR2=SEQ ID NO: 100, and H-CDR3=SEQ ID NO: 24). Appropriate correction is required.

Claim 45 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 43. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). SEQ ID NO: 89 (recited by claim 43) is identical to SEQ ID NO: 425 (recited by claim 45). Therefore, there are no embodiments within the scope of either claim 43 or 45 which are not encompassed by the other.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-9, 11-16, 22, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims are broadly drawn to antibodies, which comprise a very large number of different combinations of claimed CDR sequences or fragments thereof

The specification discloses only particular combinations of the 6 CDR sequences will result in antibodies that bind to antigen as claimed (see e.g. Table 1, pp.64-68). The specification does not describe antibodies that comprise random combinations of the CDR sequences encompassed by the claims (and fragments thereof), i.e. the examiner is unable to find any support in the disclosure as-filed for the claimed antibodies that comprise random combinations of the CDR sequences and fragments thereof. Applicants are required to cancel the new matter in the response to this Office action. Alternatively, applicants are invited to identify sufficient written support in the original specification for the "limitations" indicated above.

Claims 1-5, 7, 8, 9, 11-16, 22, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies that comprise 6 CDRs, wherein: L-CDR1 comprises SEQ ID NO: 96, L-CDR2 comprises SEQ ID NO: 97, L-CDR3 comprises SEQ ID NO: 18, H-CDR1 comprises SEQ ID NO: 99, H-CDR2 comprises SEQ ID NO: 100 and H-CDR3 comprises SEQ ID NO: 24 (i.e. the 6 CDRs of the elected MSR-7 antibody) or that comprise the particular combinations of antibodies disclosed in Table 1 of the specification, does not reasonably provide enablement for an antibodies that contain any other combination of the CDRs recited by independent claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The claims are broadly drawn to antibodies or fragments thereof, which comprise a very large number of different combinations of claimed CDR sequences.

The specification discloses only particular combinations of the 6 CDR sequences will result in antibodies that bind to antigen as claimed (see Table 1, pp.64-68). The specification does not enable antibodies that comprise random combinations of the CDR sequences encompassed by the claims (and fragments thereof), i.e. the specification does not teach that the artisan can pick and choose different combinations of the claimed CDRs and still produce an antibody that binds antigen as claimed. Further, the specification does not teach that any random combination of the CDRs as claimed will also comprise the sequences encompassed by claims 4 and 5. Thus, the specification does not enable to the full scope of the claims.

As stated previously, it is well established in the art that the formation of an intact antigen-binding site of all antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope (Paul, citation U on PTO-892 dated 28 January 2008, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions"). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of

heavy and light chain variable regions is required in order to form functional antigen binding sites (Paul, page 293, first column, lines 3-8 and line 31 to column 2, line 9 and lines 27-30). Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (citation V on PTO-892 dated 28 January 2008, page 1979). The Rudikoff reference teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that the antibodies and fragments thereof as defined by the claims, which may contain less than the full complement of CDRs from the heavy and light chain variable regions have the required binding function. Applicants have provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability of producing an antibody and fragments thereof containing random combinations of the CDRs encompassed by the claims, thus resulting in an antibody that retains the antigen specificity currently claimed. However, as stated previously, the claim language also reads on small amino acid sequences, which are incomplete regions of the variable region of the antibody and which do not necessarily bind antigen, i.e. the "fragment thereof" of claim 1 and dependent claims does not require antigen binding. One of skill in the art would neither expect nor predict the appropriate functioning of the antibodies as broadly as is claimed.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such

guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Therefore, in view of the lack of guidance in the specification and in view of the discussion above, undue experimentation would indeed be required to use the invention commensurate with the scope of the claims.

Claim 7 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 is directed to the antibody molecule of claim 1, wherein said antibody is selected from the group consisting of MSR-7 and an affinity-matured version of MSR-7. The invention employs novel biological materials, specifically the MSR-7 antibodies. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the specific biological materials and it is not apparent if the biological materials are readily available to the public. It

appears that applicants have not deposited the biological materials, and a deposit at a recognized depository may be made for enablement purposes.

In the reply filed on 02 July 2008, applicants assert that the specification sets forth the amino acid sequences (and encoding nucleic acid sequences) of the variable regions of MSR-3, MSR-7, and MSR-8 antibodies, e.g. at p.14, lines 16-20 and lines 24-27. Applicants assert that with the disclosure of both the amino acid and the encoding nucleic acid sequences, a person skilled in the art may readily construct the MSR-3, MSR-7, and MSR-8 antibody molecules. Furthermore, applicants assert that the six CDRs of affinity-matured versions of the antibodies are disclosed, for example, in Table 1. Thus, applicants assert that affinity-matured versions may also be readily reproduced. Accordingly, applicants assert that the specification disclose repeatable processes for obtaining the biological material as set forth in claim 7.

Applicants' arguments have been fully considered and are not found persuasive. Claim 7 clearly encompasses the actual monoclonal antibodies, not just any antibody comprising the recited sequences. Antibodies are defined not only by their small antigen-binding regions, but also by the remainder of their structure. The process of producing monoclonal antibodies is unpredictable; even when a small antigen is used multiple different monoclonal antibodies can be produced. See for example Kuby (1997. Immunology, Third Edition, pp.131-134), which teaches the process by which monoclonals are produced. See also Alberts et al. (1994. Molecular Biology of the Cell, 3rd Edition, pp.1216-1220), which teaches the three-dimensional structure of antibodies is complex. Note

particularly the large models on pp. 1219-1220 which indicate that the antibody molecules are comprised of hundreds of amino acids. The structure of a large protein such as an antibody is dependent not just on the antigen-binding region, but on the totality of the interactions of the hundreds of amino acid residues. Furthermore, Alberts teaches that the constant domains of the antibodies determine certain properties of the antibodies (see for example p.1217, final paragraph).

The specification fails to disclose the complete sequence and structure of the MSR-7 antibody and affinity-matured versions of the MSR-7 antibody, which is encompassed by claim 7. The art recognizes that specifying the sequence of the variable region alone is not sufficient to determine the entire structure of an antibody, and that making monoclonals is an unpredictable process. Monoclonal antibodies are so unique that a skilled artisan cannot simply construct one, the actual hybridoma which secretes the antibody must be present in order to make it. Thus deposit of said hybridoma is required for compliance with § 112, first paragraph. MPEP § 2404.02 recognizes that when undue experimentation would be required for an artisan to make a biological product, deposit can be required. The examiner has concluded that in order to make the actual antibody MSR-7 and affinity-matured versions thereof, the hybridoma is required.

Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC

§112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification lacks sufficient deposit information for the monoclonal antibody MSR-7. Because this monoclonal antibody is unknown, and therefore, publicly not available and cannot be reproducibly isolated from nature without undue experimentation, a suitable deposit for patent purposes is required.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be **irrevocably removed** upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

For the reasons above, it would not be possible for the skilled artisan to make the antibodies recited in claim 7. Therefore the rejection is maintained.

Conclusion

Allowable Subject Matter

Claims 41-43 and 46-49 are allowable. It is noted that the antibody of claims 41-49 is is not a naturally occurring product. Said antibody is a recombinant antibody, which is not naturally occurring and must be produced by one skilled in the art.

Claims 1-5, 7-9, 11-16, 22, 29 and 30 are rejected.

Claims 1-5, 7-9, 11-16, 22, 29, 30 and 45 are objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The

fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G.E./

Gregory S. Emch
Patent Examiner
Art Unit 1649
24 April 2009

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
April 27, 2009